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Preventing Iron Deficiency in Women and Children

Technical Consensus on Key Issues

unicef

A UNICEF/UNU/WHO/MI Technical Workshop

Preventing Iron Deficiency in Women and Children:

Background and Consensus on Key Technical Issues and Resources for Advocacy, Planning and Implementing National Programmes

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Acknowledgements

This report is a joint effort of a group of experienced international health workers and eminent scientists and professionals who participated in a UNICEF/UNU/WHO/MI Technical Workshop designed to reach a consensus on issues that can accelerate and expand national programmes for the prevention of ID (iron deficiency). The workshop was organized at the request of the United Nations Administrative Committee on Coordination/Sub-committee on Nutrition (UN ACC/SCN) with a goal of providing a resource to accelerate iron deficiency control programmes by clarifying technical issues.

The Technical Workshop and overall process of developing this report were organized on behalf of the United Nations University (UNU) by the Iron Deficiency Programme Advisory Service (IDPAS) of the International Nutrition Foundation (INF). The Micronutrient Initiative (MI) and the Nutrition Section of the United Nations Children's Fund (UNICEF) headquarters provided close, ongoing professional and logistical support as well as financial assistance.

An initial working draft of the report was prepared by IDPAS based on a draft done by Joanne Csete from UNICEF with input from Jenny Cervinskas and Venkatesh Mannar from MI, and Fernando Viteri of the University of California. The meeting participants, listed at the back of this document, included many of the scientists and policy makers responsible for the research reports and guidelines used in the working draft. Among those not present whose work contributed substantially were Michele Dreyfuss, Stuart Gillespie, Leif Hallberg, Richard Hurrell, Penelope Nestel, and Rebecca Stoltzfus.

Over three days in October 1998, participants discussed and redrafted each section of the working paper and then presented revised sections in plenary for further revision leading toward consensus statements in 10 areas. Drafts of an "action agenda" and "executive summary" were also developed.

From the IDPAS project and UNU, Nevin Scrimshaw served as chairman throughout the workshop and Gary Gleason was overall rapporteur. For post-meeting editing, detailed review and comments or suggestions came from George Beaton, Joanne Csete from UNICEF, Bruno de Benoist and colleagues from WHO, Leslie Elder from the MotherCare III Project, Ian Darnton-Hill from Helen Keller International (HKI), Wilma Freire from the Pan American Health Organization (PAHO), Sean Lynch from the Veterans' Administration Medical Center in Hampton, Virginia, USA, Glen Maberly from the Program Against Micronutrient Malnutrition (PAMM), Alex Malaspina from the International Life Sciences Institute (ILSI), Barbara Macdonald from the Canadian International Development Agency (CIDA), Jenny Cervinskas, Venkatesh Mannar, and colleagues from MI, Milla McLachlan and colleagues at the World Bank, Nancy Sloan from the Population Council, and Fernando Viteri from the University of California. Alison Greig (MI) contributed importantly to the editing.

Marc Kaufman of Desktop Publishing and Design Co., Newton, MA, USA developed the publication design.

The report often borrows from, and sometimes builds upon, the dedicated work of many nutrition specialists and national officials and programme officers who are initiating and developing stronger programmes to prevent iron deficiency in women and children around the world. All of these persons, as well as the other participants at the Technical Workshop, have contributed in a major way to this report. Its dissemination and use respond to the 1998 UN ACC/SCN request that consensus be developed on several issues to promote development of more effective public health programmes to prevent iron deficiency in children and women around the world.

Nevin S. Scrimshaw, *Workshop Chairman*
Gary R. Gleason, *Rapporteur*

Executive Summary

Iron Nutrition Needs Greater Attention

Iron deficiency and its anaemia affect more than 3.5 billion people in the developing world (1), stealing vitality from the young and old and impairing the cognitive development of children. There have been increased efforts to develop improved interventions involving food fortification and oral iron supplementation, and calls for programmes that link the use of fortification, supplementation and dietary education in a combined strategy to prevent and control iron deficiency (ID). However, too little progress has been made toward the global elimination of iron deficiency. Iodine and vitamin A deficiencies receive far greater attention and support. Part of the reason for this lack of action is the fact that iron deficiency anaemia (IDA) has few overt symptoms. There is a lack of widespread knowledge of its serious and often permanent consequences to the cognitive development of young children, and its negative impact on the health of all people.

Iron Deficiency has Massive Economic Costs

Iron deficiency has a massive, but until recently almost totally unrecognized, economic cost. It adds to the burden on health systems, affects learning and school performance, and reduces adult productivity. The World Bank, WHO, and Harvard University list iron deficiency anaemia as having a higher overall cost than any other disease except tuberculosis (2). Iron deficiency anaemia can usually be prevented at low cost, and the benefit/cost ratio of implementing preventive programmes is recognized as one of the highest in the realm of public health.

Economic analysis supports political commitments made by heads of state at the World Summit for Children in 1990 and the International Conference on Nutrition in 1992 where they agreed to implement national actions to reduce micronutrient deficiencies in their populations.

Interventions and Programme Partners are Available

Recognition of the problem of iron deficiency and its consequences is seriously out of balance with the current availability of solutions effective in preventing it, and over 50 per cent of the world population suffers the consequences. Iron deficiency is truly a global epidemic that requires urgent action. Unless populations eat a diet rich in vitamin C and/or meats, consume iron fortified foods, and/or take iron supplements regularly, many individuals will be found to be iron deficient at different stages in their life cycles. Greatly increased commitment on the part of national governments is required to solve the problem, as is the support of international and bilateral agencies, and NGOs. It will also require commitments from communities, private institutions, the food industry, and the mass media.

New Programme Actions are Required

Since 1990, outstanding progress has been made toward eliminating iodine deficiency through universal salt iodization. Vitamin A deficiency is being addressed through nationwide biannual distribution of vitamin A capsules to infants, young children, and women postpartum, as well as fortification of foods, and the promotion of dietary behaviour change. During this same period, little progress has been made toward the global elimination of iron deficiency, in part, because it is a hidden deficiency with few overt symptoms. While individual women are frequently aware of their anaemia, policy makers and service providers often fail to recognize the significance of the problem at the public health level. Advocacy and national scale programmes have been constrained by the erroneous perception that effective, practical interventions are not available.

Consensus on Technical Issues

In recognition of these problems, the United Nations Administrative Committee on Coordination/Sub-committee on Nutrition (UN ACC/SCN) proposed that an effort be made to expand and accelerate programmes to prevent iron deficiency in children and women by clarifying a number of technical issues. The UN ACC/SCN suggested that a Technical Workshop review issues related to the iron fortification of foods, oral iron supplementation, and dietary education aimed at improving iron nutrition, and recommend ways that these and other interventions be integrated to build overall effective programmes to prevent iron deficiency.

This document grew from a process that initially reviewed recent research and analyzed constraints on public health programmes that use one or more types of intervention to improve iron nutrition and prevent iron deficiency. It draws together information published in guidelines developed at several workshops as well as from the scientific and field programme experience of organizations active in country efforts to address and prevent iron deficiency. Thirty nutrition programme specialists and scientists from international agencies, universities, and NGOs met for three days in October 1998 to discuss and revise the initial draft, moving toward consensus on several technical issues. The October consultation was followed by two additional rounds of revisions based on written comments from participants and their organizational colleagues. The Iron Deficiency Programme Advisory Service (IDPAS) of the International Nutrition Foundation (INF) in close collaboration with MI and UNICEF undertook overall responsibility for revision and writing the current document.

Several important issues are summarized and technical points clarified through sets of consensus statements. Outlined are several points that can be used to support advocacy, accelerate planning, and strengthen implementation of programmes to prevent iron deficiency. The document attempts to address many commonly heard questions regarding iron nutrition and to point to other more detailed guidelines and sources of up-to-date technical information. The report also outlines action points for organizations working to assist in advocacy and programme design at various levels. At the end, sections provide references and sources of relevant guidelines, research, and technical information, as well as the addresses of a number of major organizations and networks that support national efforts to prevent iron deficiency.

Areas of Consensus

Assessment and the integration of multiple interventions are needed

While each country requires an initial assessment of the magnitude of its iron deficiency and anaemia problems, much of the information needed for a rapid assessment of the extent is often readily available. Where interventions are indicated, guidelines are now available to help plan more effective efforts to prevent iron deficiency and control anaemia. The food processing industry, health sector, education sector, employers, community groups, and the mass media should participate in the programme planning process. Decisions will be required on how various interventions can best be phased in, and on how they should interact. Also important are considerations of the time it is likely to take to build the highest feasible level of effectiveness around each type of intervention, and for a combined and integrated intervention package.

Specialists at the Technical Workshop agreed that the use of a single type of intervention would likely be insufficient to solve the problem of iron deficiency for all the groups within a single population that have differing iron needs. Stronger consensus—not only within this group, but also at the UN ACC/SCN, and in several regional consultations on iron deficiency—continues to be needed on how to appropriately integrate intervention strategies that promote dietary change, initiate food fortification, broaden use of supplementation, and control infections contributing to anaemia.

Food fortification

There is growing consensus, based on the long established experience of many industrialized countries and more recent policies in growing numbers of middle income and poorer countries, where populations are iron deficient, it is desirable to fortify food staples (such as wheat and maize flour), or condiments (such as soy sauce, fish sauce, sugar, and salt) with iron. Agency representatives and participating specialists at the Technical Workshop emphasized that significant amounts of iron can be safely delivered to most iron deficient population groups through fortification of staple foods, and that this can be done in a highly cost effective and sustainable manner. While general fortification of food staples such as wheat, maize meal, or rice is not likely to be sufficient to significantly reduce iron deficiency in infancy and early childhood, the specific iron fortification of complementary foods for infants and young children has been shown to be effective.

Successful introduction of food fortification with iron requires active involvement of key groups from the food processing industry as well as from the health sector, the government agencies setting standards for food additives, and often other groups. Fortification has a strong political appeal in terms of cost effectiveness and long term sustainability.

Oral supplementation

The specialists at the Technical Workshop recognized that while food fortification can and should be the primary approach to improve the underlying iron nutrition status of populations, fortification alone is not adequate for meeting iron requirements at all stages in the life cycle. Pregnancy and late infancy are two periods of life where oral supplements are most often needed to prevent iron deficiency anaemia.

When the prevalence of anaemia in pregnant women in a population is 40 per cent, which is common in many developing countries and several in transition, recent guidelines from the International Nutritional Anaemia Consultative Group

(INACG), WHO, and UNICEF call for urgent action including universal distribution of iron supplements to pregnant women. These guidelines were endorsed by participants at the Technical Workshop, with agreement that during pregnancy and for two months postpartum women should receive daily supplementation with iron and folic acid. Where anaemia prevalence is high, iron supplements should also be given to women of childbearing age and to children between six and 18 months of age under conditions that can assure the intake of the supplements.

Programmes to combat iron deficiency should include iron supplementation of anaemic women during pregnancy and aim toward having all women enter pregnancy having good iron stores. For nonpregnant women of childbearing age and young children, the UNICEF/UNU/WHO/MI Technical Workshop participants recognized that pilot studies of weekly administration of iron tablets have been promising.

Communication for dietary change

It was agreed among participants that countries with public health problems of iron deficiency should promote dietary improvement as a part of an integrated strategy to prevent iron deficiency, but that this cannot be expected to solve the problem on its own. It is important to learn of those commonly consumed foods and meals that contain iron and promote its absorption, and then to promote more use of these in family diets. However, iron nutrition improvement based on dietary promotion is generally limited because the iron availability in vegetables is poor and attempts to increase meat consumption, with its better-absorbed iron, are often met by economic and sometimes religious constraints.

Integration with public health programmes

There was consensus that interventions of national programmes to prevent iron deficiency should be integrated for better and more sustained impact, and that such interventions are mutually beneficial to other public health programmes. Especially encouraged were programmes concurrently addressing other micronutrient deficiencies and the control of infections such as hookworm and schistosomiasis that cause blood loss.

It was agreed that reproductive health programmes could be usefully linked to the prevention of iron deficiency through promotion of healthy child spacing that reduces the burden of pregnancy on a woman's iron status. Important links between breastfeeding promotion and prevention of iron deficiency in infants and women were identified. Although breastmilk is not high in iron, the iron it contains is highly absorbable. Moreover, exclusive breastfeeding delays menstruation, providing an infertile period after birth during which a woman can more easily build iron stores. The new Integrated Management of Childhood Illness (IMCI) programmes need to be closely linked to iron deficiency prevention efforts and included in updated modules on the treatment of anaemia in young children.

Safety

On issues related to the safety of iron fortification and supplementation, participants agreed with the recent technical consensus of other expert groups, as well as WHO and UNICEF. The participants agreed that iron supplements can be given safely and effectively to risk groups including pregnant women with iron deficiency anaemia in malaria endemic areas. The weight of these endorsements should remove a common constraint on broadening the use of supplements in many programmes. The safety of iron supplements and iron fortification where persons have thalassemia was clarified based on the results of a recent expert meeting regarding this issue.

Better monitoring, evaluation and research

Additional work on improving effectiveness of iron deficiency control programmes is required using the results of better monitoring, evaluation, and research. There was agreement that all intervention programmes should incorporate appropriate monitoring processes, evaluation of their impact, and widespread dissemination of information on lessons learned. More information is needed on the effectiveness of fortification and on the lessons learned by many countries starting to use this intervention. Such information must be made more widely available to international agencies and non-governmental organizations (NGOs).

Better tools and more information are needed to allow programmes using iron supplements to identify factors that negatively affect their effectiveness and to guide such programmes toward better systems of pill distribution and higher levels of compliance in the regular taking of iron supplements. Data are also required to support nutrition programme advocacy and to allow programme leaders to optimize operations and resource use. Collection and analysis of more field-generated data are also necessary to facilitate decisions on new recommendations by organizations such as WHO and UNICEF.

Conclusions

The group concluded that the interventions necessary to make a difference in reducing the prevalence of iron deficiency and iron deficiency anaemia in the populations of most countries are available, affordable, and sustainable. Technical issues should no longer be seen as a constraint on programme advocacy and design. However, there was also a consensus that more work must be done to identify and develop the various subcomponents of interventions needed for effective large-scale programmes. Particular effort is also required to set up, evaluate, and share information on lessons learned in the field about programmes based on integrated "packages" of interventions and multiple sector participation.

More clearly defined and better-resourced commitments are needed from national governments, donors, NGOs, and groups able to provide technical assistance to programmes designed to prevent iron deficiency and iron deficiency anaemia. This will require increased and active advocacy and engage-

ment of the highest national political level. Public and private sector collaboration, especially with the food industry is important as well. Stronger, better focused international and national commitment is now needed to initiate, accelerate, and expand programmes to prevent iron deficiency in women and children; thus protecting their health and development and providing them with their basic rights.

SECTION 1

Workshop Background, Goals, and Recommendations

Technical Workshop Background

Despite stated national and international commitments, the level of national activity and international support for current programmes for the control and prevention of iron deficiency among vulnerable population groups has not been commensurate with the prevalence, seriousness, and consequences of this public health problem. Stronger expert consensus on technical issues was among the factors identified by the Iron Working Group of the Subcommittee on Nutrition (SCN) of the UN Administrative Committee on Coordination (ACC) needed to accelerate and strengthen advocacy, planning, and implementation of larger and stronger iron deficiency prevention programmes. Another factor was the need to disseminate information more broadly on resources available for national level advocacy, and for several technical aspects of programme planning and implementation.

To build stronger consensus the Iron Working Group called for:

> *"A Technical Workshop to resolve issues using a practical, field-oriented, science-based approach be held before the next meeting of the Working Group. The report of this workshop will be presented at next year's Working Group meeting.* (3)*"*

Nutrition and programming specialists working with UNICEF, the Iron Deficiency Programme Advisory Service (IDPAS) of the International Nutrition Foundation (INF)[†], and the Micronutrient Initiative (MI)[††] developed a draft working paper and organized the requested workshop. In preparation for the workshop and to provide initial focus for discussions, the working paper was organized around several technical issues, with a major set of recent references and lists of contacts for organizations providing technical assistance in the field of preventing iron deficiency.

The initial working paper, as well as most meeting discussions, relied heavily on the MI/UNICEF report **Major Issues in the Control of Iron Deficiency** edited by S. Gillespie (1998) (4), the INACG/WHO/UNICEF **Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anaemia** by R. Stoltzfus and M. Dreyfuss (1998) (5), portions of the IOM document, **Prevention of Micronutrient Deficiencies: Tools For Policymakers and Public Health Workers.** C. Howson, E. Kennedy, A. Horwitz, (eds.) (1998) (6), and the Micronutrient Initiative Report on **Micronutrient Fortification of Foods: Current Practices, Research, and Opportunities** (1996) by M. Lotfi, V. Mannar, et al. (7), and the WHO/UNICEF/UNU report, **Indicators for Assessing Iron Deficiency and Strategies for its Prevention** (in press, 1999) (8). The working paper, workshop discussions, and this report also drew from regional guidelines for control of iron deficiency anaemia developed with the support of UNICEF, WHO, PAHO, and other organizations. Several recently reported research studies, reports of other relevant meetings and workshops, and the expert knowledge, research, and programme experiences of invited participants were also used. The working paper with references was sent to all invited participants prior to the Technical Workshop.

Thirty specialists came together for the Technical Workshop at UNICEF Headquarters in New York,[†††] 7–9 October

[†] The INF manages funding for and executes several research and editorial activities of the Food and Nutrition Programme of the United Nations University. The INF organized the Technical Workshop and led development of this report in consultation with the sponsoring agencies.

[††] The Micronutrient Initiative (MI) is an international secretariat established to reduce micronutrient malnutrition. It is funded primarily by the Canadian International Development Agency (CIDA), the International Development Research Centre (IDRC), UNICEF, USAID, and the World Bank. MI provided funding and technical support for organization of the Technical Workshop, and development of this report.

[†††] Participants were experienced nutrition scientists and/or specialists in the design of public health nutrition programmes working with noted universities, UN and Government agencies, specialized projects, and NGOs.

1998. The initial goal was to complete discussions and work on consensus statements for the final report during the meeting. This document consists, in major part, of revisions made to the preliminary working document by participants during the Technical Workshop but also through two rounds of additional revisions. Subsequent drafts were shared with all participants and attempts were made by IDPAS specialists to incorporate a balanced representation of comments from participants that allowed consensus on most issues to be maintained.

The Consensus Report

This document is drawn from the review and consensus of the participants at the Technical Workshop, utilizing information from a number of major recent reviews, overviews, and research studies on iron deficiency and iron deficiency anaemia stressing practical considerations for public health intervention. Each section of the document consists of a central theme with background information followed by the consensus statements agreed by Technical Workshop participants. Each theme covered is relevant to advocacy for the decisions and actions needed to accelerate and strengthen programmes to prevent and control iron deficiency. A set of "Actions to Expand and Accelerate Programmes to Prevent Iron Deficiency," found at the end of this section, was developed by participants to assist nutrition and public health policy makers and specialists in national governments and major NGOs who are guiding programme advocacy, planning, and implementation at various levels. Readers are strongly encouraged to make use of the guidelines and technical materials that are listed in Annex I of this document.

The Technical Workshop participants recognized the value and encouraged the use of several sets of practical, action-oriented guidelines related to preventing iron deficiency and controlling iron deficiency anaemia that have recently been developed. These provide comprehensive coverage of approaches to reduce iron deficiency. Where possible and appropriate, information from recent guidelines and technical documents has been used to illustrate or reinforce a specific point in the background sections.

During discussions at the Technical Workshop and in subsequent comments, participants also emphasized that effective planning of programmes to prevent iron deficiency requires an analysis of the specific situation and environment where the programme will operate.

This document is not intended to replace or repeat information in existing publications, but to complement them as an additional resource in developing a national analysis of situations related to iron nutrition, conducting advocacy with the highest level of policy makers, and developing new and potentially more effective programme strategies and interventions.

Listings of current guidelines, research reports, and technical literature as well as organizations, projects, specialists, and networks offering guidance, technical assistance and other resources for policy makers and intervention planners concerned with preventing iron deficiency are provided in the last sections of this report.

Intended Audiences and Objectives

The main audiences for this document are national government officials responsible for setting public health and nutrition intervention priorities, and programme planners in international and bilateral development assistance organizations, government agencies, and NGOs. The document points toward clear, affordable actions that can be taken to prevent and reduce iron deficiency in populations where it is a problem. It should be noted that the topics covered in this document relate mainly to the prevention and control of iron deficiency in the context of public health policy and programme development. They are not oriented toward, or intended to guide, the clinical treatment of individuals with moderate or severe iron deficiency anaemia.

This effort seeks to bring additional clarity to several important issues that have been the focus of excellent work of many organizations and groups. Several of the technical issues being clarified in this document point toward innovative approaches to prevent iron deficiency in vulnerable groups, such as children and women, that are moving from controlled trials toward large-scale use. The effectiveness of such programmes needs evaluation under operational conditions.

Perceived Constraints to Expanding Intervention Programmes

Iron deficiency is well recognized as the most widespread of the nutritional deficiencies of current public health importance. In addition, there are now well-developed models showing the major economic costs both to health services and to the lost productivity associated with iron deficiency and iron deficiency anaemia. Nonetheless, intervention programmes targeted to prevent and control anaemia have lagged in the establishment of goals in planning and in implementation. For several reasons, iron has become known in professional circles as the "neglected nutrient."

Several factors have constrained advocacy and development of effective interventions to prevent iron deficiency. The focus on iron malnutrition has normally been only on anaemia. Even among health professionals, there has been little concern for the well-documented fact that iron deficiency is a systemic condition adversely affecting most body functions. In addition, most public health goals concerning iron malnutrition focus only on the prevention and treatment of iron deficiency anaemia in pregnant women and fail to even recognize either the serious consequences of iron deficiency to infants and young children, or the need to ensure that women enter pregnancy with good iron stores.

Even for iron supplementation of pregnant women, most national protocols call only for supplementation in the second and third trimesters. This is too late to allow the buildup of iron stores needed to prevent deficiency during a period where good health is critically important. In general, neither the extent of

the public health problem of iron deficiency nor its consequences for pregnant women, infants, young children, adolescents, and women of childbearing age is well understood by most public health policy makers in either developing or developed countries. For example, the Goals of the World Summit for Children call for the reduction of iron deficiency anaemia in women by the year 2000 to one-third of 1990 levels. At that time there was no call for any actions to be taken against iron deficiency in young children or adolescents. In 1996, the UNICEF/WHO Joint Committee on Health Policy (JCHP) expanded the focus to include prevention of iron deficiency in young children, adolescents, and pregnant women where iron deficiency anaemia is a problem. Still, in recent discussions among the leaders of programmes in UNICEF, there was recognition that end-of-decade goals for reducing iron deficiency will not be met and that new, accelerated, and more effective actions are urgently needed.

New and stronger programmes to prevent iron deficiency are also constrained by the fact that many working in public health still are unaware of the well developed technical guidelines aimed at guiding interventions to *prevent* rather than treat iron deficiency and iron deficiency anaemia, nor are many aware of the excellent projects and organizations providing technical assistance in this area.

Iron supplementation recommendations in particular have been too long defined in terms of a clinical treatment approach rather than a public health approach stressing prevention. This has led to confusion among programme planners and public health personnel.

Some policy makers and clinically oriented scientists have been concerned that public health interventions aimed at increasing iron intakes of those in vulnerable population groups, through fortification of staple foods and/or encouraging the use of oral iron supplements for specific groups, might be disadvantageous to populations. From a public health perspective, the evidence does not support this concern (see Sections on *Fortification and Oral Supplementation*).

New Potential to Accelerate and Expand Interventions

There is now clear evidence that simple, low-cost tools and methods for assessment of the problem in populations, and feasible, sustainable, and effective intervention models are available, as is knowledge of the adverse consequences of iron deficiency in various vulnerable groups. A number of recent publications and reports contain most of the relevant information and guidelines needed to develop and implement programmes based on such models.

The value of any set of guidelines is limited, however, until there is acceptable consensus on a number of key issues that have constrained the acceleration of advocacy, planning, and funding of programmes to prevent and reduce iron deficiency in vulnerable groups. The Technical Workshop compiled and, where possible, harmonized the recommendations of recent documents, reviewed recent research and field experiences, and developed a series of authoritative consensus statements on programme issues related to preventing and controlling iron deficiency.

Consensus on a number of the issues related to iron deficiency about which there have been technical disputes, were reached on the basis of existing evidence and the need to accelerate the development of programmes. The issues discussed and presented represent most areas where there is scientific or programmatic debate or frequent questions raised by national programme planners, practitioners, researchers, and/or policy makers in countries needing major efforts to control iron deficiency, as well as among those agencies that might support such efforts.

Actions to Expand and Accelerate Programmes to Prevent Iron Deficiency

The Technical Workshop developed and recommended several actions that can accelerate, improve, and expand programmes to prevent iron deficiency. These complement other recommendations found in several sets of guidelines and consultation reports listed in Annex I.

Advocacy

1. Promote agreement among the international agencies on establishing a high priority for the prevention of iron deficiency wherever it is a public health problem.
2. Emphasize in advocacy messages the facts that iron deficiency is not only a major public health problem but also it seriously hampers human resource development.

   Include the facts that anaemia:

   - damages child development
   - causes intelligence quotient losses similar to iodine deficiency
   - costs countries through productivity losses, educational losses, and increased morbidity
   - kills when anaemia is severe.
3. Direct significant advocacy efforts to initiate national efforts to prevent iron deficiency toward national political leaders, emphasizing that: the legal obligation of governments to assure good iron nutrition and prevent the damage done to individuals' health and development by iron deficiency is a matter of internationally agreed children's, women's, and basic human rights; stress the potential political value of leading an effort to set a national policy of universal iron and folic acid fortification of staple foods.
4. Emphasize that iron deficiency is a systemic condition affecting vulnerable groups including infants, young children, adolescents, and women of childbearing age—not just a problem of anaemia in pregnancy.
5. Make it very clear that feasible and cost effective interventions are available for preventing iron deficiency wherever it occurs.
6. Emphasize that preventing and controlling iron deficiency is an issue that goes far beyond the health sector.
7. Point out the highly recommended intervention of food fortification requires major involvement from the food industry.

Coordination

1. Build on existing efforts and infrastructure in many regions for promoting the control of iron deficiency and avoid duplication.
2. Promote coordination among the international agencies within a country to avoid conflicts in programme efforts for the control of micronutrient deficiencies.
3. Use the consensus of this workshop and related documents to enhance and improve efforts for the control of iron deficiency.
4. Promote wider dissemination and greater use of existing technical information and guidelines that are needed to build interventions and make them more effective.

Design and Intervention

1. Assure that iron deficiency anaemia is recognized as a serious public health problem among women and young children.
2. Assume that where malaria is not endemic, the primary cause of iron deficiency is insufficient bioavailable dietary iron. Even where malaria is a major problem, programmes to prevent malaria should be linked with those to prevent iron deficiency in children and women because, in general, the stages of development of public health and socioeconomic development in such areas are not satisfactory and the population is at high risk for iron deficiency.
3. Design public health interventions for preventing iron deficiency based on an assessment of the situation that emphasizes the feasibility of the major programme elements.
4. Where iron fortification is feasible, position this intervention so that it serves as the entry point for a strategy mix because fortification can reduce the prevalence of iron deficiency in a sustainable manner for all sectors of the population while making other interventions more effective.

Continued

Actions to Expand and Accelerate Programmes to Prevent Iron Deficiency *(continued)*

Effective Interventions

1. Determine the best available delivery mechanisms for each specific strategy: fortification, supplementation, and dietary improvement including involvement of programme partners inside and outside the health sector.
   - Involve leaders of the food industry as early as possible in discussions of iron fortification of foods.
   - Involve the community in the planning and development of operating programmes.
   - Utilize non-health sectors as well as the health sector for managing supplementation.
   - Clearly define the role of each organization in the support of strategies.
2. Provide a strong communication component based on a realistic appraisal of population characteristics and patterns of food consumption to support the mix of strategies.
3. Incorporate appropriate public health interventions along with the mix of strategies for preventing iron deficiency, including prevention and control of helminthic infections causing blood loss, promotion of breastfeeding, timely and appropriate complementary feedings that provide iron, and child spacing measures.

Strengthen Technical Support

1. Establish stronger technical advisory and assistance capacity to support the needs of countries for help in programme development and operation.
2. Promote interagency and inter-country cooperation in information exchange and capacity building.
3. Develop guidelines for appropriate situation analyses.
4. Convene multi-country, multi-sector workshops that include health and nutrition leaders as well as legislators, to develop action plans, encourage cross-sector cooperation, and generate peer pressure for their implementation.

Monitoring and Evaluation

1. Assure proper monitoring and reporting of the impact of both fortification and supplementation initiatives.
2. Document the effectiveness of programmes to promote dietary behavioural change favouring improved iron status.
3. Share lessons learned and evaluation results both with those working on country programmes and with the international community.
   - Use existing international databases and the communication channels of projects dedicated to improving micronutrient nutrition to share information and lessons relevant to intervention and programme effectiveness.
   - Assure that national capacity building is an integral part of programme monitoring and evaluation activities.

Priority Areas for Research

1. Determine the effectiveness of various approaches involving community participation and the use of mass media and non-formal education channels to build sustainable support for iron deficiency prevention and control programmes.
2. Evaluate the practicality and effectiveness of proposals for small-scale and community-based fortification of foods.
3. Determine whether weekly supplementation of children and women of childbearing age is effective in large-scale operational programmes where compliance is, by necessity, unsupervised.
4. Determine the long-term effect that preventive supplementation has on the iron reserves of nonpregnant women and the impact these reserves have on iron nutrition during pregnancy.
5. Obtain reliable information on the costs of the various interventions for the prevention and control of iron deficiency and iron deficiency anaemia.

Distinguishing Anaemia, Iron Deficiency, and Iron Deficiency Anaemia

Iron status can be considered as a continuum (see Figure 1) which results from long term negative iron balance where iron stores are progressively lost. While approximately 73 per cent of the body's iron is normally incorporated into haemoglobin and 12 per cent in the storage complexes ferritin and haemosiderin, a very important 15 per cent is incorporated into a variety of other iron-containing compounds, some of them enzymes of vital importance. The haem iron compounds include myoglobin, cytochromes, catalases, and peroxidases. The non-haem iron compounds include NADH and succinic dehydrogenases; xanthine, aldehyde, and alphaglycerophosphate oxidases; phenylalanine hydroxylase; and ribonucleotide reductase. Alphaglycerophosphate oxidase, for example, shuttles electrons across the mitochondrial membrane. Also important are the iron-dependent enzymes proline and lysine hydroxylase, and a number of others including enzymes involved in DNA replication. When iron intake no longer meets the need of normal iron turnover and pathological iron losses and stores are exhausted, there is a decrease in transferrin saturation and an increase in transferrin receptors on the surface of cells in all types of tissue throughout the body. When the depletion is sufficient to affect haemoglobin synthesis, anaemia results (see Box 1 with haemoglobin and haemocrit cutoff levels defining anaemia).

A fact often under emphasized is that all stages of iron deficiency anaemia are only a subset of the spectrum of iron deficiency. When individual haemoglobin levels are below minus two standard deviations of the distribution of haemoglobin in an otherwise normal population of the same sex and age, and living at the same altitude, iron deficiency anaemia is considered to be present; 2.5 per cent of a normal population would be expected to be below this threshold. In other words, iron deficiency anaemia represents a subset of iron deficiency at the lower end of the distribution. The prevalence of iron deficiency anaemia in a population,

BOX 1

Haemoglobin and Haematocrit Cutoffs Used to Define Anaemia in People Living at Sea Level

Age or Sex Group	Haemoglobin Below g/dL	Haematocrit Below (Per cent)
Children 6 months to 5 years	11.0	33
Children 5–11 years	11.5	34
Children 12–13 years	12.0	36
Nonpregnant women	12.0	36
Pregnant women	11.0	33
Men	13.0	39

Source: "**Indicators for Assessing Iron Deficiency and Strategies for its Prevention**," WHO/UNICEF/UNU, in press (8).

BOX 2

Definitions of Anaemia, Iron Deficiency, and Iron Deficiency Anaemia

Anaemia

Abnormally low haemoglobin level due to pathological condition(s). Iron deficiency is one of the most common, but not the only cause of anaemia. Other causes of anaemia include chronic infections, particularly malaria, hereditary haemoglobinopathies, and folic acid deficiency. It is worth noting that multiple causes of anaemia can coexist in an individual or in a population and contribute to the severity of the anaemia.

Iron Deficiency

Functional tissue iron deficiency and the absence of iron stores with or without anaemia. Iron deficiency is defined by abnormal iron biochemistry with or without the presence of anaemia. Iron deficiency is usually the result of inadequate bioavailable dietary iron, increased iron requirement during a period of rapid growth (pregnancy and infancy), and/or increased blood loss such as gastrointestinal bleeding due to hookworm or urinary blood loss due to schistosomiasis.

Iron Deficiency Anaemia

Iron deficiency when sufficiently severe causes anaemia. Although some functional consequences may be observed in individuals who have iron deficiency without anaemia, cognitive impairment, decreased physical capacity, and reduced immunity are commonly associated with iron deficiency anaemia. In severe iron deficiency anaemia, capacity to maintain body temperature may also be reduced. Severe anaemia is also life threatening.

Source: R. Yip and S. Lynch (defined during the Technical Workshop, UNICEF Headquarters 7–9 October 1998).

therefore, is a statistical rather than a physiological concept. It reflects only that proportion of the population with iron deficiency severe enough to impair erythropoesis.

Iron deficiency anaemia is considered to be present in a population only when the prevalence of haemoglobin below the cut-off is greater than 5 per cent. Moreover, the evidence indicates that the prevalence of iron deficiency is double that of iron deficiency anaemia.† Therefore, when iron deficiency anaemia rates are above 50 per cent, the entire population is likely to be iron deficient.

Because anaemia is the most common indicator used to screen for iron deficiency, the terms "anaemia," "iron deficiency," and "iron deficiency anaemia" are often used interchangeably. However, prior to the development of iron deficiency anaemia, there are mild to moderate forms of iron deficiency where various cellular functions are impaired (see Box 2)

The occurrence of iron deficiency anaemia cannot be accounted for by dietary iron intake alone. Dietary factors in food that inhibit or enhance iron absorption require consideration as do other factors associated with blood loss, including schistosomiasis and hookworm infection, and haemorrhage during delivery or due to trauma (see Section 4). Although iron deficiency accounts for most of the anaemia in underprivileged environments, there are other causes of anaemia including other nutritional causes like vitamin B_{12} and folic acid deficiencies. There are also anaemias associated with malaria due to red blood cell breakdown, and those related to genetic disorders such as sickle cell anaemia, thalassemia major (originally "Mediterranean anaemia"), and abnormal haemoglobins. As iron deficiency anaemia prevalence decreases, other causes of anaemia may become proportionately more important, but excepting sickle-cell anaemia in some populations of African decent, none are at levels requiring a public health response. Successful iron supplementation results in the disappearance of anaemia as a public health problem, except where malaria is highly prevalent.

† Recently, questions have been raised concerning the appropriateness of the WHO blood haemoglobin standards that define iron deficiency anaemia, its levels of severity and the designation of appropriate populations and specific cut-off levels for serum ferritin. These issues may require consideration by an expert committee convened by WHO to address them.

Figure 1: Iron Status in Humans, Selected Measures, Metabolic and Clinical Manifestations and Risks

Iron Status

Lower ← → *Higher*

	Anaemia	Iron Deficiency	Iron Depletion	Normal Iron	Increased Iron Stores*
Marrow Iron Stores	0	0	0–trace	2–3 +	3–4+
Plasma ferritin (µg/l)	< 10	10	< 20	100 ± 60	> 250
Plasma iron (µg/l)	< 40	< 60	< 115	115± 50	> 150
Iron Protoporphyrin (µg/dl RBC)	200	30	30	30	30
Transferrin saturation (%)	< 10	< 15	< 30	35± 15	> 50
Metabolic Manifestations	Impaired cognition	Impaired cognition**	None	None	Possible parenchymal tissue damage *** Possible increased cardiac risk***
	Compromised immune function	Compromised immune function**			
	Reduced skeletal muscle function and physical capacity	Impaired skeletal muscle function**			
Clinical Manifestations	Fatigue	Increased infections**	None	None	Mild to severe illness***
	Weakness				
	Increased infections				
Risks	Pregnant women • Increased mortality • Infant with low iron stores				With usual intakes of iron from diet fortification and supplementation, this is not a risk in normal individuals because of efficient autoregulation of iron absorption

Sources:

* Iron Overload is said to exist when total body iron is in excess of 4 grams. Haemochromatosis is a term used to describe the clinical disorder that results in parenchymal tissue damage from iron overload. Haemochromatosis may occur when there is an inappropriate increase in the intestinal absorption of iron found in homozygotes with hereditary haemochromatosis or with chronic blood transfusions. The danger of haemochromatosis lies in the fact that excess iron deposits are stored not only in macrophages but also in hepatocytes, cardiac cells, endocrine cells, and other parenchymal tissue. These excess iron deposits interfere with normal functions of these cells or may even cause cell death. In haemochromatosis, the serum ferritin is high and serum iron saturation of transferrin sometimes approaching 100 per cent (9).

** Depending on severity.

*** In rare individuals who are homozygous haemochromatosis and who have high iron intakes or cases of chronic transfusion therapy.

Source: Modified from Herbert V. Anemias. *Clinical Nutrition.* Paige, O.M. (ed). Mosby Philadelphia, PA, USA.

Programmes to Prevent Iron Deficiency

Background

Iron deficiency is costly and its prevention is highly cost-efficient

The growing advocacy for programmes to prevent and control iron deficiency is based in part on the strong economic arguments that effective interventions to prevent iron deficiency anaemia are among the most cost-effective available to policy makers in public health and nutrition. Economic analysis demonstrates the importance of these programmes to policy makers in agencies, to ministerial and parliamentary leaders who deal with resource allocations, and to the leaders of agencies and private sector firms necessary for financial support. Information on the cost-effectiveness of interventions provides programme advocates with information that complements data on the health and developmental impact of iron deficiency (4), and reinforce the moral and legal obligations of governments to address this issue based on human rights.

The WHO/World Bank-supported analysis of *Global Burden of Disease* ranked iron deficiency anaemia as the third leading cause of loss of disability-adjusted life years (DALYs) for females aged 15-44 across the globe (2). Among men in this age group, iron deficiency anaemia is ranked among the top 10 disease burdens globally, reflecting the debilitating effects of anaemia even in this group. This factor was more important globally than war-related death and disability, and nearly as important as the global scourge of tuberculosis, according to this analysis.

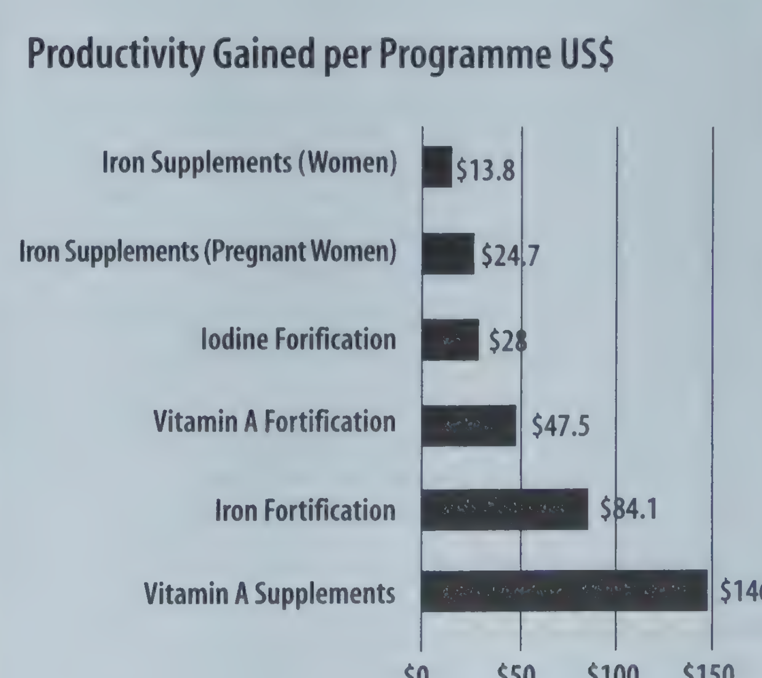
Using different but equally compelling criteria, USAID produced a 1994 analysis estimating that in South Asia, a two-thirds reduction in anaemia would result in a US$3.2 billion increase in agricultural production over the seven-year period 1994–2000 (10). On the effectiveness of education that analysis noted, "control of iron deficiency anaemia improves attitudes, capacity to concentrate, and school attendance (10)."

While cost analyses are normally highly specific to site, situation, and specific programme goals, such studies can often allow useful comparison of various interventions.

The USAID paper used World Bank data to compare various micronutrient programmes in terms of productivity gained per dollar spent based on research(11) (see Figure 2). All interventions were cost-effective, with iron fortification second in number of dollars gained for each dollar spent. Vitamin A supplements were highest because of the large number of productive years assumed to be gained by reducing vitamin A-related mortality in children less than five years of age. However, this referred only to countries in which subclinical vitamin A deficiency is still a health problem.

A recent paper prepared by the Micronutrient Initiative on the "Economic Consequences of Iron Deficiency" (12) ana-

Figure 2: Relative Cost Effectiveness of Micronutrient Interventions



Adapted from Levin, World Bank, 1991 (11).

lyzed relationships between anaemia and several economically quantifiable factors including:

- lower future productivity of children;
- lower current productivity of adults;
- costs for care of low birth weight and premature infants;
- costs of maternal mortality;
- other consequences on growth;
- decreases in immunity and increased absenteeism due to infectious disease;
- increases in morbidity and mortality;
- greater susceptibility to heavy metal toxicity.

Algorithms were developed to estimate economic losses from iron deficiency-related factors. Based on 15 country examples, the mean value of productivity losses due to iron deficiency was estimated at around US$4 per capita, or 0.9 per cent of gross domestic product (GDP). This amounted to approximately US$5 billion annually in South Asia alone. As such, an integrated package of interventions to prevent iron deficiency, including food fortification and iron supplementation could be highly cost-effective.

The cost of iron supplements and fortificants per individual is low. However, as with any public health programme taken to national scale and focused beyond treatment to prevention, overall costs of supplies, shipping, distribution, training, communication materials, monitoring, and applied research become substantial.

More work on costs and cost-effectiveness is needed, not only for further advocacy support for new programmes, but also to help guide field staff in developing effective and efficient sustainable programmes. Information on costs of current and new programmes can also be extremely useful. For example, using UNICEF prices, the tablet costs for women receiving one year's supply to be taken daily during pregnancy and initial lactation is less than US$1.00. The World Bank estimates that the overall cost for daily iron supplementation per pregnancy is US$2.50. The 1998 UNICEF price for 1000 tablets of 200 mg ferrous sulphate (60 mg elemental iron) plus 400 μg folic acid was US$2.70 (or US$.0027 per tablet). The cost-effectiveness of programmes for children less than one year of age, currently being supplemented with a liquid-based supplement, and that of the programmes aimed at preventing iron deficiency anaemia in pregnant women by supplementing all women of childbearing age have not been determined systematically. The cost of elemental iron as a food fortificant is less than US$0.04 per person per year.

Awareness of the high prevalence and serious effects of iron deficiency in children and women is growing

WHO estimates that iron deficiency anaemia affects more than 50 per cent of pregnant women in the world and 46 per cent of children under two years of age (4). Such percentages are much higher if only the developing world is considered. Surveys in most developing countries indicate a 50-60 per cent anaemia prevalence among women and children, most of it due to iron deficiency. Iron deficiency anaemia affects adult men as well, mainly because of iron losses due to hookworm. For example, this is the case in up to 30 per cent of men in the lowlands of Guatemala, and similar prevalence rates have been reported for male tea pickers in Sri Lanka and rubber plantation workers in Indonesia (13–15).

By any reckoning, iron deficiency anaemia is a serious public health problem in nearly all developing countries and in subpopulations of industrialized countries as well. Recently, national Demographic and Health Surveys (DHS) supported by USAID, as well as others conducted by the US Centers for Disease Control (CDC) and UNICEF, have begun to measure anaemia levels in national populations. Experts now agree that advocacy in many countries and development of programmes to combat iron deficiency need not await the completion of nationally representative or other large-scale surveys. The results of such studies have reinforced the general finding that levels of anaemia in pregnant women are usually similar to anaemia levels of children less than five years of age in the same population. Experience indicates that where there is significant poverty—even in industrialized countries—there is a strong chance of iron deficiency in vulnerable groups, and that interventions are needed.

Human rights obligations require micronutrient actions

The evidence of a significant reduction in labour productivity of anaemic adults is well established, as is the adverse health impact of anaemia on women and children, including impairment of cognitive function. Beyond issues of economics and lost productivity, national obligations to control and prevent iron deficiency have grown out of a variety of international human rights agreements that generate legal as well as moral obligations for governments to take active steps to prevent and control anaemia in women and children.

Iron deficiency anaemia prevention reduces circumstances of HIV/AIDS transmission

Anaemia control is a critical factor in promoting comprehensive maternal health in areas—particularly in some African countries—where HIV is the primary threat to maternal health. Preventing severe anaemia lessens the possible need for blood transfusion that might introduce the HIV virus and may help to maintain immunity to superimposed infections in persons with the disease.

Control of malaria, hookworm, and other micronutrient deficiencies and public health efforts should be a part of iron deficiency anaemia prevention programmes

Where these infections, such as malaria and hookworm, are endemic, WHO and UNICEF recommend that actions to control these infections become important elements in

population-based programmes to prevent and control iron deficiency anaemia. In areas where malaria and iron deficiency are both prevalent, integrated iron deficiency and malaria control strategies are essential (see Section 9).

Effective programme links can also be set up between efforts to prevent and control iron deficiency anaemia and those aimed at preventing other micronutrient deficiencies as well as with programmes aimed at improving environmental sanitation and personal hygiene, maternal and child health services, family planning and the promotion of breastfeeding.

Concerns about iron overload should not constrain programmes to prevent iron deficiency through fortification and/or supplementation

The recently widely distributed MI/UNICEF publication, *Major Issues in the Control of Iron Deficiency*, edited by Stuart Gillespie includes a comprehensive annex, "The Practical Significance of Iron Overload for Iron Deficiency Control Programmes." There are subsections on "excessive iron absorption from a normal diet," "hereditary haemochromatosis," "iron loading anaemias," "sub-Saharan iron overload," "iron accumulation from blood transfusions," "iron overload and iron fortification," "iron status and coronary heart disease," and "excess iron and infections." This publication is highly useful for programme personnel working on advocacy and planning interventions to prevent iron deficiency because it provides authoritative answers to common clinically based concerns about the effect of iron interventions on susceptible individuals (4). In the interest of avoiding considerable redundancy, the reader of this document is referred to that of Gillespie for more comprehensive information on iron overload.

Regarding the specific interventions outlined to reduce iron deficiency, there has been concern that iron supplementation could have an adverse effect on some individuals, although it is generally accepted that with fortification this is much less likely. Fortunately, iron absorption in normal individuals is extraordinarily well regulated so that as iron stores increase, absorption decreases, and the normal individual is protected from iron overload (16).

Haemoglobinopathies are clinical diseases that result from genetically determined abnormalities of haemoglobin molecule structure or synthesis (9), e.g., sickle cell disease, and some cause haemolysis. Thalassemias are conditions in which normal globin chain synthesis is defective, causing ineffective erythropoiesis and haemolysis. Ineffective erythropoiesis is associated with excessive iron absorption. In addition, persons with this condition often need medical management including blood transfusions providing haem iron.

Patients with thalassemia minor and other haemoglobinopathies' traits do not absorb iron excessively. They may have coexistent iron deficiency and respond to iron to the extent that the lowered haemoglobin is due to iron deficiency.

The regular blood transfusions needed by individuals with thalassemia major contribute massive amounts of iron that require iron chelation therapy to prevent iron overload. Once the haemoglobin level of thalassemics is stabilized, the normal down-regulating mechanism for dietary iron absorption will function again (4). It is estimated that 100–200 thousand individuals are born with thalassemia major every year. Thalassemia is not a reason to curtail or delay development of programmes to fortify staple foods such as wheat flour with iron (see Box 3).

Hereditary haemochromatosis is an autosomal recessive genetic disorder of iron metabolism in which those who are homozygous have defective regulation of iron absorption (see note at bottom of Figure 1 also). From 0.25 per cent to 0.35 per cent of populations of European origin are homozygous for haemochromatosis. However, not all homozygotes manifest the disorder (9). Heterozygotes may develop moderately increased iron stores but no clinical disease.

A recent series of studies indicates that the presence of the C282Y mutation of the HLA-H haemochromatosis gene, which when homozygous, is responsible for more than 90 per

BOX 3

Recommendations on Iron Fortification and Thalassemia from the WHO Eastern Mediterranean, Middle East, and North Africa

Thalassemia major and thalassemia minor are single-gene recessive inherited blood disorders characterized by the defective production of haemoglobin.

Thalassemia major is a serious life threatening condition that normally manifests itself after six months of age. Without treatment those affected usually die of infection or heart failure in the first years of life.

Thalassemia minor can very closely resemble mild anaemia. No treatment is necessary unless iron deficiency is present. Iron stores in people with thalassemia minor are normal, and dietary manipulation is unlikely to have a significant effect. People with thalassemia minor are not at risk of iron overload and are not at any greater risk of complications from iron in the diet than anyone else in the general population.

Conclusions

- Thalassemia major is a serious condition that requires treatment with regular blood transfusions and iron chelation.
- Thalassemia minor is a condition not affected by dietary inputs.
- There is no reason to believe that flour fortification will have any significant adverse impact on those individuals suffering from thalassemia major.
- Flour fortification will have a significant and beneficial effect on the people who suffer from iron deficiency and its anaemia including those with thalassemia minor.

Source: Adapted from: **Report of a WHO Eastern Mediterranean, Middle East, and North Africa Regional Consultation**, 1998.

cent of hereditary haemochromatosis, is found in people of Celtic decent and is very rare outside of populations of Northern European origin. No examples of the C282Y mutation have been found in any of the African countries studied (Algeria, Ethiopia, and Senegal) (17).

A non-HLA-linked genetic abnormality has been suspected (gene not identified) of causing iron overload among the Bantu group of Southern Africa. However, this is doubtful since it appears only in a mostly male subgroup that consumes large quantities of a low-alcohol, acidic local beer produced in iron pots and containing large amounts of highly bioavailable iron (100-200 mg/dl).

Iron status and infections

Iron is essential for a number of important immune mechanisms including leucocytic killing power, T-cell types and numbers, leucocytic mitogenic response to antigens and delayed cutaneous hypersensitivity (18). The withholding of iron from infectious organisms by the strong iron-binding capacity of transferrin and lactoferrin is an important defense mechanism. There is no evidence that iron-fortified foods or iron supplementation affect this mechanism. Reports of increases in morbidity related to iron administration are based on large therapeutic doses of iron given to severely malnourished individuals whose immune systems are greatly compromised. Field studies of daily iron supplementation consistently show a decrease in morbidity from infections, particularly diarrhoeal and respiratory diseases. Oral iron supplementation given to persons with hookworm infections can improve haemoglobin status despite continued blood loss (19).

Another argument sometimes raised as a reason not to approve iron fortification or iron supplementation is the claim that it could increase prevalence rates of coronary heart disease. A U.S. National Academy of Sciences overview states that there is currently no epidemiological evidence to support this hypothesis (20). Similarly, there have been claims that iron overload is a risk factor in some cancers. The same study concludes that: "there is no valid evidence for a role of iron exposure, whether by diet or other routes, in the etiology of human cancer" (20).

Consensus Statements

1. The firm conclusion from several analyses is that iron deficiency anaemia carries costs to all countries, but its effect on the economic productivity in developing countries is enormous. The estimate that iron deficiency anaemia is responsible for the loss of about one per cent of gross domestic product (GDP) (about US$4 per capita per year) does not include the burden of maternal death associated with severe anaemia and the lowered effectiveness of funds spent on education. The costs to the health system for the treatment of anaemia, and of an increase in infections are also substantial.

2. Cognitive deficits in children constitute a major economic burden of iron deficiency anaemia. However, this remains largely unrecognized as a real cost to economic and social development. In the face of evidence, and given the existence of feasible and cost-effective interventions to address the problem, the case for urgent action is compelling.

3. The consequences of iron deficiency, coupled with obligations mandated under various international conventions on human, women's, and children's rights, place a legal and moral burden on governments of developing countries. Reducing the burden of anaemia partially fulfills a country's moral and legal obligations to its children, women, and men.

4. Some well-developed information on the economic cost of iron deficiency anaemia is now available and should be used for accelerated action and policy development. Additional information of this type is needed, particularly on issues related to the cost effectiveness of programmes and interventions to prevent iron deficiency and iron deficiency anaemia.

5. In almost all developing countries, existing evidence is likely to be sufficient to justify, advocate, and launch interventions to improve iron status, prevent iron deficiency, and correct anaemia through integrated control programmes.

6. National health records often contain enough information about anaemia levels to justify strengthening current anaemia control efforts with emphasis on preventing iron deficiency in vulnerable groups and planning of integrated programmes. These can usually be confirmed by local surveys of vulnerable groups and by consulting local practitioners regarding responses to iron administration observed in anaemic patients to allow for advocacy to begin. Established iron deficiency anaemia rates in children and pregnant women in similar economic/cultural groups in neighbouring areas or countries can serve as an initial proxy for determining the probability that interventions are needed in groups not yet assessed.

7. In countries where child malnutrition or other nutrient deficiencies are recognized to exist, plans for any major national or subnational health and nutrition surveys (e.g., Demographic and Health Surveys (DHS), Multiple Indicator Cluster Surveys (MICS)) should add the measurement of haemoglobin to the survey to gain information on the actual levels of iron deficiency anaemia in subgroups of the population. However, such surveys are not necessary to justify greater efforts to prevent and control iron deficiency.

8. In the few countries without even limited data on rates of iron deficiency anaemia, rapid assessment of at-risk groups should be planned and supported. Established field assessment procedures are available, and low-cost equipment make such assessments affordable and cost-effective.†

9. Current assessment methods for iron deficiency anaemia are adequate for planning and evaluation purposes, and there are good training manuals for detection of anaemia in low cost settings (21, 22).

10. The use of biochemical tests designed to identify the specific cause of anaemia in all individuals is unnecessary. Serum ferritin tests are expensive, cumbersome (the collection and preservation of samples in the field), and difficult to interpret in the presence of infection and other unknown factors (see Box 4). Small therapeutic trials with the suspected causal deficient nutrient or nutrients (e.g., iron, and if the response is unsatisfactory, folic acid, and rarely, other haematopoetic nutrients) are often more economical and useful.

11. Iron overload disorders and haemochromatosis are rare, even in those populations of European origin (principally Celtic) most susceptible to them. Thus, the use of fortification and supplementation as public health interventions for preventing and controlling iron deficiency should not be constrained. Specifically:

    - There is no evidence of a health risk from iron fortification, even in industrialized country populations where most of the population receives adequate dietary iron from other sources.
    - Iron fortification of cereals and weaning foods is a safe and effective means of reducing the prevalence of iron deficiency and anaemia in a population.
    - Well-designed supplementation programmes can be effective and safe means for preventing iron deficiency when targeted to vulnerable groups in populations whose diets are inadequate in bioavailable iron. These include a large proportion of women and young children in most developing countries.

BOX 4

Drawbacks of Using Serum Ferritin Tests and Analyses for Studying the Iron Status of Populations

Serum ferritin is a reflection of iron stores and can be useful in determining iron status of a study population. However, there are very important drawbacks that limit its usefulness in field studies:

- Sophisticated laboratory equipment is needed to measure ferritin.
- Ferritin testing is expensive.
- Ferritin levels are falsely elevated in the case of inflammation or infection, masking iron deficiency or causing its prevalence to be underestimated.
- Only in the case of low values (probably less than 30 μg/l) is the testing of ferritin useful in determining iron status.
- Where chronic or repeated infections of inflammatory conditions are prevalent, ferritin values less than 30 μg/L suggest depleted iron stores, and values less than 15 μg/L are clearly indicative of iron depletion. In order to have value, the interpretation of results of ferritin testing under these conditions must take this into account.

Thus, low values indicate iron deficiency, but in the context of developing populations normal values can only be interpreted if additional laboratory tests are available. Therefore, a decision to measure ferritin in population surveys requires careful consideration of its cost effectiveness and the interpretability of the results.

† Simple and relatively low-cost methods of measuring haemoglobin and haematocrit are available for large-scale surveys. The portable testing instruments for haemoglobin levels include the "HemoCue" haemoglobin photometer available through UNICEF (approximate cost is US$200 with disposable curettes at US$35/100). CDC has a supply of HemoCue instruments that it can loan out for anaemia surveys. The "CompuTest" is a similar testing instrument produced by Bayer in Germany recommended by GTZ. Development of a non-invasive instrument capable of measuring haemoglobin levels is needed.

SECTION 3

Need for Multiple Intervention Strategies and Participation

Background

The participants in the Technical Workshop shared endorsement of the recommendation of the UN ACC/SCN and many other groups that the most effective public health approach to prevent and control iron deficiency and iron deficiency anaemia is a well-planned and monitored programme that employs multiple interventions and cross-sector strategies. A schematic for an integrated public health strategy was developed and recommended by the 1998 UN ACC/SCN Iron Working Group (see Figure 3).

There was general agreement that for all populations, including those where iron deficiency anaemia prevalence in vulnerable groups is significant (above 10 per cent), there should be programmes focusing on prevention of iron deficiency through fortification, supplementation, communication aimed at improving dietary behaviours, programme monitoring and linkage with other appropriate public health efforts.

To be effective, programmes to prevent iron deficiency need the involvement and support of high level political leadership and participation from other sectors, in addition to the health sector. For food fortification, active participation of the food industry is critical. There was agreement with a recommendation from the "Final Report on the Regional Consultation on Anaemia" in the UNICEF Eastern and Southern Africa Region (23), that sustaining anaemia prevention and control programmes require communities to clearly understand the problem and participate in decisions on appropriate strategies, programme implementation, monitoring and evaluation (23).

Development of effective, sustainable programmes to prevent iron deficiency, and the balance and integration of different interventions, will be greatly facilitated by the clarification of several intervention-related issues, and by consensus on a number of technical issues. Many such issues are covered in the sections that follow.

Consensus Statements

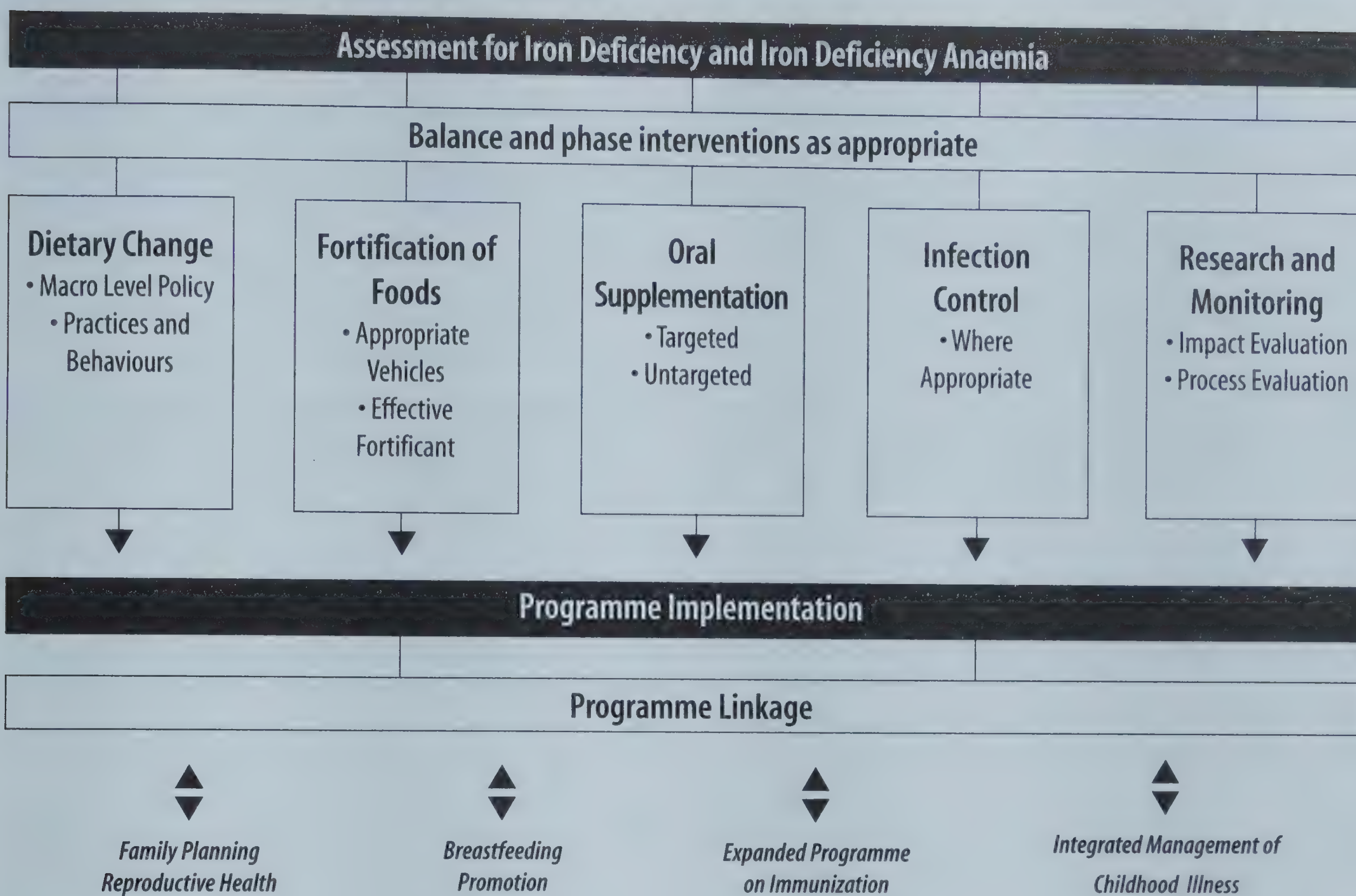
1. Iron deficiency is the most neglected and widespread of all nutritional deficiencies, constituting a vast drain on social and economic development around the world. There is a continually growing number of scientific findings showing adverse health and developmental effects related to iron deficiency and iron deficiency anaemia. Recent studies document permanent cognitive damage to children between six and 18 months of age affected by anaemia, contributing to the long-recognized tally of economic losses to families, communities, and societies as a result of iron deficiency and iron deficiency anaemia. While public health policy and programme guidelines for anaemia control exist in many countries, explicit, actionable programmes need to be developed and implemented. Many recent analyses of trends in anaemia prevalence show little improvement, comparing poorly with the progress in the control of iodine and vitamin A deficiencies.

2. In fulfillment of the Declaration of the 1990 World Summit for Children, the International Conference on Nutrition, and global commitments to enhance children and women's nutrition status, all stakeholders—national governments, international and bilateral organizations, NGOs, and the private sector—must take action to strengthen existing programmes and to develop new, integrated strategies to prevent iron deficiency and iron deficiency anaemia among vulnerable groups, particularly infants, young children, and pregnant women.

3. Better-planned and stronger advocacy efforts are needed to improve current national efforts to initiate and use integrated strategies to prevent and control iron deficiency.

4. The magnitude of the prevalence of iron deficiency and iron deficiency anaemia in infants, children, adolescents, and adults, along with their associated adverse health and

Figure 3: Schematic of Integrated Strategy for Prevention and Control of Iron Deficiency



Source: UN ACC/SCN Iron Working Group 1998 (3).

development consequences, demand that all governments and those international and bilateral organizations and NGOs concerned with health, development, and human rights give a high and immediate priority to confronting this problem. Countries should initiate strong, integrated, multi-intervention strategies and programmes to prevent iron deficiency anaemia where it is a public health problem. Programme interventions should include as a priority the most vulnerable groups, especially pregnant women and those of childbearing age, infants and young children, and adolescent girls.

5. While each country's strategy to prevent and control iron deficiency should be based on an analysis of the local situation and developed according to the severity of the problem, aetiological factors, resources, and sociocultural conditions of that country, all countries should integrate an appropriate combination of strategies.

6. Phased or simultaneous intervention programmes, utilizing multiple appropriate and complementary strategies with varying time lines for implementation will be needed to address the range of affected individuals within a population. In general:

- In most countries, initial efforts will focus on fortification of basic foods and supplementation of target groups with a high prevalence of iron deficiency anaemia.
- Development of national programmes for universal fortification of staple foods with iron will improve the iron status of everyone and lay the foundation for a sustainable, long-term source of dietary iron. Programmes of oral iron supplementation, if they can be set up in ways that are effective in allowing and assuring compliance, can address the higher iron requirements of specific groups and control iron deficiency anaemia.
- Mandatory for success is a communication component aimed at promoting improved public health and nutrition practices as well as a supportive policy environment through well-designed and powerfully delivered advocacy messages.

7. Other major programme design considerations should include:

   - Long term emphasis on the sustainable prevention of iron deficiency and iron deficiency anaemia, and special efforts to prevent women from entering pregnancy in an iron deficient state.
   - The roles of non-health sector government organizations, NGOs, the private sector, particularly the food industry, and communities.
   - Assurance of community participation, both through involvement of community leaders in recognizing the importance of the problem and also in designing and playing leading roles in activities such as promoting fortified food products, improving diets, and distributing and promoting iron supplements to high risk groups.
   - Establishment of mechanisms for effective communication from the community to the government agencies that determine agricultural, economic, and other policies affecting food costs and availability.
   - Planning for sustainability and national self-sufficiency by assuring community ownership of the interventions, and a strategic time frame for phasing out donor provision of supplements, fortificants, or other commodities.
   - Assure sufficient time within the programme to allow communication and educational strategies aimed at improving dietary intake and absorption of iron to be effective with target population groups.
   - Utilize appropriate techniques for sustaining continuous awareness of the problem, and adherence to the programme requirements.

SECTION 4

Causes of Iron Deficiency

Background

Iron deficiency has long been understood to result from the interaction of multiple aetiological factors that lead to an imbalance between the iron requirements of the body and the amount of iron absorbed (see Figure 4). The key factors responsible for iron deficiency include:

Dietary

- Low levels of iron in diet.
- Low bioavailability of iron in the diet (because of the form of iron, high prevalence of inhibitors, low prevalence of enhancers of bioavailability or some combination of these).
- Insufficient quantity of dietary iron relative to enhanced needs during specific life phases (infancy, adolescence, and pregnancy).
- Deficiencies in nutrients that are linked to iron metabolism.

Life cycle

- Repeated pregnancies.
- Bleeding associated with use of intrauterine devices (IUDs) for birth control.
- Excessive menstrual bleeding.
- Elevated needs associated with pregnancy and rapid growth in early childhood and adolescence (puberty).
- Iron deficiency in infants has an intergenerational link to iron deficiency in pregnancy.

Disease states

- Hookworm, schistosomiasis, and to a much lesser degree, trichuris, causing chronic blood loss.
- Other pathological blood losses (e.g., haemorrhoids, peptic ulcer, and other less common gastrointestinal diseases and malignancies).
- Processes that impair iron absorption and utilization: malabsorption syndromes, chronic and/or repeated diarrhoea, and rare genetic conditions.

Consequences of low socioeconomic status

- Food insecurity.
- Inadequate or lack of access to health care.
- Poor environmental sanitation and personal hygiene.

Genetic causes of anaemia

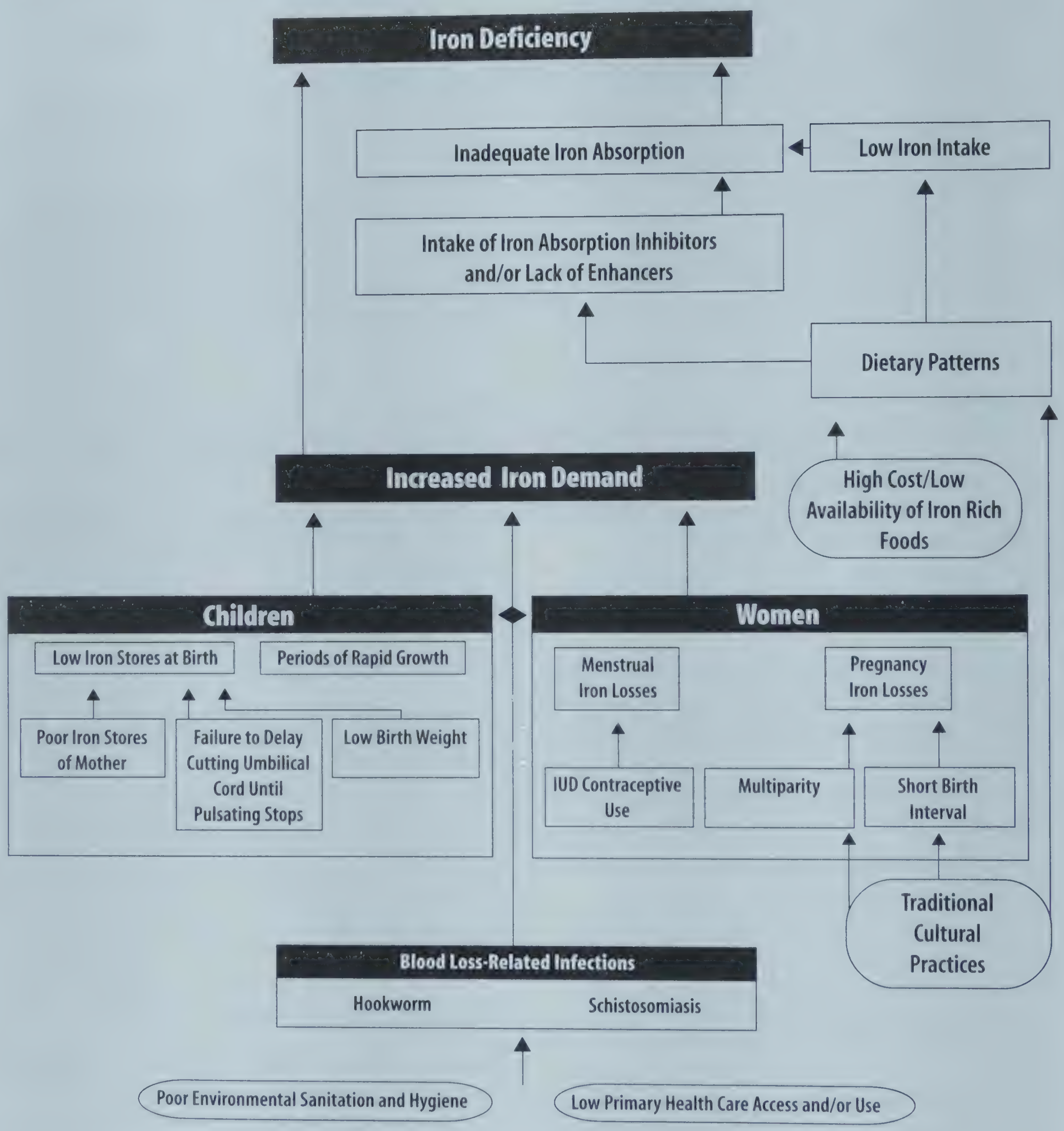
- Sickle cell disease.
- Thalassemia major.
- Other haemoglobinopathies.

Prevention of iron deficiency requires action at all levels where adequate iron stores are not being maintained

A confusing issue that often constrains support from programme decision makers for stronger programmes addressing iron malnutrition, is the emphasis only on iron deficiency anaemia without adequate understanding of the adverse effects of the subclinical forms of iron-related malnutrition.

If the emphasis for public health planners is to prevent rather than simply to treat iron deficiency anaemia, the *trigger point for action* must come when a high incidence of iron deficiency, rather than a high incidence of anaemia, is present.

Figure 4: Factors Contributing to Iron Deficiency in Children and Women



Source: Iron Deficiency Programme Advisory Service (IDPAS); International Nutrition Foundation (INF), 1999.

The shift to action at this stage is justified by research showing adverse health consequences not only to persons who are anaemic but also to those who are iron deficient (24).

As noted in the previous section, there is likely to be at least one additional case of subclinical iron deficiency for each case of iron deficiency anaemia when anaemia prevalence rates are below 50 per cent. When iron deficiency anaemia prevalence rates are above 50 per cent there is likely to be close to 100 per cent prevalence of iron deficiency. This fact, and the recognition that iron deficiency in itself has adverse health consequences, are bases for the INACG/WHO/UNICEF guidelines' recommendation that the routine use of iron (and folic acid) supplements be extended for longer periods for populations of pregnant women and children six to 24 months of age where the prevalence of anaemia is 40 per cent or greater (5).

Prior to these guidelines, according to the UNICEF/WHO Joint Committee on Health Policy (Jan. 1995) (25), the level of anaemia "triggering" universal supplementation in pregnant women was 30 per cent. The 40 per cent anaemia trigger for universal supplementation of women and children was established when nearly all developing country populations were above this figure. This is still the case for most countries, but *iron deficiency* anaemia damages the affected individual at *any* level of population prevalence. It has been customary to consider 10 per cent prevalence of a disease as a level triggering the need for public health action. Thus, neither fortification nor supplementation can be abandoned when anaemia levels fall below 40 per cent.

Iron deficiency in women of childbearing age can be expected to be significantly higher than in men based on women's monthly loss of 40–50 ml of blood during menstruation.[†] There is a subset of women (around 15 per cent) who have higher losses of blood during their menstrual cycles (80-100 ml).[††] For them, dietary intake is unlikely to provide the amount of iron they need to make up the loss. Young children and male adolescents are also at greater risk than adult males because of higher iron needs during periods of rapid growth.

Low intakes of iron and/or low iron bioavailability can be assumed if children and women are disproportionately affected compared to men (26). If the distribution of haemoglobin of all groups is skewed to the left, additional causes of anaemia, besides dietary, can be suspected (e.g., hookworm, malaria, HIV/AIDS).

Clear guidelines linking aetiology to programme decision making are needed

There has been considerable progress in developing guidelines for assessment, fortification, and supplementation interventions. Professionals developing programmes in the field continue to need better guidance on appropriate tools to interpret haemoglobin and haemocrit values, on qualitative and quantitative methods for assessment and programme monitoring and evaluation and on how better to select and use the types of commonly existing data that help determine the aetiology of iron deficiency. Such guidelines need to include strategies and information on how to relate aetiological factors and organizational issues with decisions on the design of an intervention. Major work is needed on guidelines that will allow those working with programmes to prevent iron deficiencies to better identify and measure factors that positively and negatively affect the effectiveness of these programmes, and on how to apply what is learned elsewhere.

Iron deficiency occurs when the amount of iron absorbed over extended periods of time is insufficient to meet physiological needs, including those imposed by pathological conditions (for example, hookworm infection). Both the actual quantity of iron intake and the bioavailability of a given intake, are important.[†††] There is agreement that the most practical and cost-effective means of determining whether anaemia is the result of iron deficiency is to measure changes in the haemoglobin or haemocrit status in response to oral iron supplementation (26).

Dietary assessment, while an indirect and limited approach for establishing levels of iron nutrition in a population, can be useful in determining overall dietary iron intake and identifying common dietary patterns that may enhance or inhibit iron absorption. Information on meal composition and dietary patterns is essential to explain interactions between iron intake and absorption enhancers and inhibitors. However, such assessments are limited for several reasons:

- limited information on meal composition in many countries;
- difficulties in obtaining reliable data on the diets of children (particularly during the weaning phase) (27);
- problems related to interviewer training and data recording;
- estimates of total dietary iron intake are misleading if this iron is poorly absorbed.

Iron absorption assessment

The quantity of bioavailable iron in the diet can be estimated on the basis of the total iron content and the prevalence of inhibitors and enhancers of iron absorption (see Box 5).

The impact of enhancers and inhibitors is particularly important where foods high in phytate or tannin are commonly consumed. High phytate foods include maize, legumes, whole wheat, brown rice, and unmilled sorghum and millet. High tannin (polyphenol) foods include tea and coffee. Absorption

[†] Where men are heavily exposed to hookworm infection this may not be true.

[††] This subset is genetically determined (mothers who suffer from iron deficiency tend to have daughters in this category) and increases with parity above three.

[†††] Bioavailability refers to the availability of a substance from the diet for use in normal metabolic processes and functions, and is influenced by both dietary and host-related physiological factors.

of iron from iron-containing foods eaten in the presence of high tannin foods may be as low as 1 or 2 per cent.

The per cent of absorbable iron in foods can be roughly estimated using an FAO/WHO model that classifies diets in terms of low (5 per cent), intermediate (10 per cent), and high (15 per cent) iron availability (28) (see Box 5).

There are a number of recent articles and guidelines that can assist in assessing the bioavailability of iron in relation to overall meal composition and various supplements that may be taken. For example, 100 mg of vitamin C taken with a "regular" meal was found to increase non-haem iron absorption by 1.7 times (30). Additional quantitative algorithms are available (4), as is an inexpensive software programme that estimates both the availability of iron from diets and the probability that observed iron intake is inadequate to maintain normal iron stores or prevent anaemia. Food frequency questionnaires and market surveys can also be useful.[†] A market survey can be done to collect information about the supply and costs of iron-rich foods (31).

Rapid assessment procedures

Rapid assessment procedures (RAP), characterized by focused interviews, and direct and participatory observation, can be used to obtain qualitative information on individual, family, and community dietary and cultural practices, and on the economic factors related to food selection and dietary choice (32, 33). Such information is needed to design effective educational strategies and messages aimed at improving dietary practices in the community and home, to develop better strategies to assure compliance with supplementation schedules, and to learn the potential value of fortifying specific foods.

Health records including the results of tests screening for HIV, blood tests for malaria, and of stool examination for helminths are often available. Their review can provide information on the prevalence of infections that contribute to iron deficiency and anaemia.

[†] A simplified dietary assessment tool has been developed recently in Tanzania and field tested. This food frequency questionnaire has a reference period of seven days, and besides collecting data on dietary iron intake, includes questions related to tea drinking and consumption of foods high in iron absorption inhibitors. (Contact: UNICEF Regional Office for Eastern and Southern Africa, Nairobi Kenya).

BOX 5

Examples of Diets with Estimated Overall Bioavailability of Iron and Substances that Inhibit or Enhance Iron Absorption

Examples of Diets with Estimated Overall Bioavailability of Iron

Typical Diet	Bioavailability of Iron
Cereal-based, roots or tubers, and legumes with negligible meat, fish, or ascorbic acid-rich foods.	Low (5% absorption)
Cereal-based, roots or tubers, with negligible quantities of food of animal origin or containing some ascorbic acid or a diet with still higher levels of animal source foods or ascorbic acid but also large amounts of tea or coffee consumed with meals.	Intermediate (10% absorption)
Diversified diets containing generous quantities of meat, poultry, and fish and/or foods containing high amounts of ascorbic acid.	High (15% absorption)

Substances that Inhibit or Enhance Iron Absorption

Absorption Inhibitors	
Active Principle	*Food Source*
Phytates	Cereals, legumes, nuts, and high levels of tea and coffee consumption with meals.
Proteins	Legumes, some animal protein sources such as milk and eggs.
Calcium and Phosphate	Milk.
Absorption Enhancers	
Active Principle	*Food Source*
Ascorbic and other organic acids	Fruits and raw or lightly cooked vegetables.
Animal tissue	Meat, poultry, and fish.

Sources: Adapted from "Examples of Diets with Estimated Overall Bioavailability," Table 6. p. 38, FAO/WHO 1988 (28), cited in Major Issues in the Control of Iron Deficiency, S. Gillespie, MI/UNICEF, 1998 (4) and Blum, M. "Overview of Iron Fortification of Foods, Proceedings: Interventions for Child Survival," Nestel P. (ed.), 1995. OMNI/USAID Project of John Snow Inc., Arlington, VA, USA, p. 45 (29).

Haemoglobin measurement

The recent inclusion of haemoglobin measurements as part of the national Demographic and Health Surveys (DHS), and the recommendation by the UN ACC/SCN that haemoglobin assessment becomes part of all major population surveys concerned with health and nutrition, has already led to findings of a high prevalence of anaemia in many countries, and this information has been used to advocate effectively for new and stronger efforts to prevent and control iron deficiency anaemia (34). Further consideration of the correlation between haemoglobin measurements, demographic, and other variables (multiparity, educational levels, rural-urban differences, type of birth control, etc.) have contributed to understanding the aetiology of iron deficiency in subpopulations of pregnant women and children (35, 36).

There are useful health information records and dietary intake data in most countries as well as a variety of research studies and other information that can form a basis for initial analysis of iron deficiency epidemiology. These allow basic decisions to be made about issues such as the value of universal or targeted fortification† and supplementation, effective food vehicles for fortification, and the need for nutrition and health education to support iron deficiency interventions and to promote the prevention and control of infections.

In most countries successful advocacy for new and stronger programmes to prevent and control iron deficiency and programme preparation will take some time. This time interval should be utilized to gain additional information for designing integrated programmes for the prevention and control of iron deficiency and iron deficiency anaemia.

Consensus Statements

1. Where anaemia prevalence rates are high enough to be a public health issue, it is rarely necessary to attempt to differentiate between iron deficiency anaemia and anaemia due to other causes. Even where other factors are significant, iron deficiency will be the main cause, either alone or in combination with other causes. The partial exception is in populations where malaria is common (see Section 9).

2. Information about possible causal factors of the iron deficiency can often be found in existing data sources. Before conducting field surveys or other new assessments, the first steps should be to search for, and assess, relevant existing information. Consideration of known causes in populations with similar relevant characteristics can be useful. Factors that should be taken into account relate to diet, stage in a life cycle, prevalence of infections and other causes of blood loss, and pathological conditions that interfere with absorption and utilization of iron. Factors related to dietary choices, economic and cultural factors, and educational levels may also contribute.

3. Causes of anaemia that can coexist with or aggravate iron deficiency anaemia include other dietary deficiencies (folic acid, vitamin B_{12}, and riboflavin), life cycle factors including folic acid deficiency during pregnancy and particularly during lactation, chronic infections, HIV/AIDS,†† malaria, malignancies, severe protein-energy malnutrition,††† haemodilution during pregnancy,†††† haemoglobinopathies, thalassemia, and acute blood loss (haemorrhage). Vitamin A deficiency also contributes to iron deficiency anaemia (19).

4. The assessment of the causes of anaemia should seek to cover the above factors, bearing in mind that it can collect programmatically useful information. This will make it feasible to initiate actions that will strengthen programmes without the need to implement separate surveys. Assessment that is intended to characterize the problem of anaemia does not have to be based on a national representative sample, but can use samples of study areas representing different ecological settings. Rapid assessment procedures (RAP) can be used to gather information more quickly and reliably on some of the above factors.

5. In areas where hookworm, malaria, and other conditions causing anaemia are known to be important public health problems, the prevalence of iron deficiency can be assumed and interventions to prevent and control these diseases should be integrated with those to address iron deficiency. However, the presence of any of these public health problems does not require a modified approach to the prevention of iron deficiency.

6. Programme advocacy and the planning and implementation of some actions to alleviate iron deficiency need not wait for exhaustive dietary surveys. However, the detailed design of effective, integrated programmes for preventing and controlling iron deficiency anaemia requires information about the levels of iron nutrition in a population, and for fortification purposes, information about specific food

† Targeted fortification programmes include use of fortified foods for specific groups of children (refugees, children in institutions, women factory workers, children in school breakfast and lunch programmes, etc.).

†† HIV/AIDS, other chronic infections and malignancies do not usually cause iron deficiency. They cause the "anaemia of chronic disease" which is a cytokine mediated disorder characterized in part by normal or increased iron stores and impaired iron release from those stores.

††† In kwashiorkor total circulating haemoglobin is reduced because of marked reduction in body mass and the need for carrying oxygen to the tissues. Iron deficiency anaemia is frequently superimposed on kwashiorkor. Because the immune system of the child with kwashiorkor is seriously compromised and too early administration of iron could allow rapid replication of infectious agents, iron administration should be delayed until initial recovery has taken place. Improvement in haemoglobin usually occurs with initial protein therapy because some haemoglobin synthesis is impaired by the deficiency.

†††† Haemodilution is the pregnancy-related physiological expansion of plasma volume in relation to red blood cells (and haemoglobin) mass, leading to lower haematocrit and haemoglobin concentrations that do not constitute anaemia.

vehicles. The types of useful information include overall iron intakes, meal composition, dietary patterns that may enhance or inhibit iron absorption (presence of inhibitors or enhancers of iron absorption in the meals commonly consumed), local perceptions about which commonly consumed foods/meals contain anaemia related nutrients. Surveys should be designed to facilitate subsequent monitoring and evaluation.

7. The variety of methods available to collect information on iron nutrition in a population include population-based surveys that provide information about the iron intake by a population and data related to the availability of the iron (37). Effective but under-utilized algorithms are available to adjust iron intake values to values of absorbed iron (31, 37). Dietary patterns and meal composition are as important as overall intake of iron in accounting for the amount of iron absorbed.

8. Existing knowledge and experience and dietary assessments usually provide useful and necessary information to guide decision making about programmes, including:

   - Selection of appropriate foods for fortification, levels of iron to be added, and the type of iron compound to be used.
   - Development of effective educational strategies and messages based on formative evaluation and qualitative research.
   - Effective advocacy for programmes.
   - Appropriate food sources of iron that are also rich in other micronutrients that are likely to be in short supply in diets.

Consequences of Iron Deficiency

Background

There have been numerous guidelines and articles indicating that iron deficiency and iron deficiency anaemia are harmful to development and health throughout the life cycle. Health and cognitive impairment problems are noted for infants and young children, adolescents, women of reproductive age, pregnant women, adults, and the elderly.

Infants and young children

- Infants born of mothers with iron deficiency anaemia are more likely to have low iron stores and to require more iron than can be supplied by breastmilk at a younger age (25).
- There is convincing evidence linking iron deficiency anaemia to lower cognitive test scores (38) and that these effects can be long lasting. Compared to most other public health problems, little emphasis has been placed on this issue or on allocation of resources to prevent and control iron deficiency anaemia in these groups.

Children, adolescents, and adults

- There are numerous studies showing a relationship between iron deficiency and/or iron deficiency anaemia and muscle function, physical activity, workplace and school productivity, and mental acuity and concentration in older children and adults.
- There is an increased susceptibility to heavy metal (including lead) poisoning in iron deficient children (25).

Pregnant women

- Iron deficiency during pregnancy is extremely common even among otherwise well-nourished populations.
- Iron status at the beginning of a pregnancy is a strong determinant of haemoglobin concentration and iron status at the end of that pregnancy.
- Severely anaemic pregnant women are at greater risk of death during the perinatal period (39).

All persons

- Iron deficiency can impair cognitive performance at all stages of life (25).
- Morbidity from infectious diseases is increased in iron deficient populations (8), and correcting iron deficiency can result in decreased morbidity (40).
- With severe anaemia, the ability to monitor and regulate body temperature when exposed to cold is reduced.
- Physical work capacity is significantly reduced in persons with iron deficiency (19, 40).

As outlined in the INACG/WHO/UNICEF Guidelines, the prevention of iron deficiency has benefits to each of these population groups as well (see Box 6).

Consensus Statements

1. Severely anaemic women are at greater risk of death. Iron deficiency is the major contributory factor to severe anaemia in pregnancy.
2. Birth weight is the primary determinant of an infant's iron status at the time of birth. Low Birth Weight (LBW) infants need iron supplementation from two months up to at least 18 months of age.
3. In countries where blood transmitted diseases, such as HIV/AIDS or hepatitis, are public health problems, the blood supply is often contaminated. Prevention of anaemia

is likely to reduce the need for blood transfusions and therefore the risk of infection transmission.

4. To promote maternal health and adequate iron stores in infants, anaemia control programmes should favour interventions that ensure that women enter pregnancy without being iron deficient and ensure that they do not become so during pregnancy.
5. There is good scientific evidence from community-based studies that iron deficiency anaemia is associated with impaired performance on a range of mental and physical functions in children. These include mental development, physical coordination and capacity, cognitive abilities, social and emotional development, and school achievement. The precise effects vary with the age groups studied.
6. Iron supplementation at a later age may not reverse the effects of moderate to severe iron deficiency anaemia that occurred during the first 18 months of life (5, 41).

BOX 6

Benefits of Preventing Iron Deficiency

In addition to economic benefits, there are strong positive benefits of effectively preventing iron deficiency.

Benefits to Children:

- Improved behavioural and cognitive development
- Where severe anaemia is common, improved child survival

Benefits to Adolescents:

- Improved cognitive performance
- In girls, better iron stores for later pregnancies

Benefits to Pregnant Women and their Infants:

- Decreased low birth weight and perinatal mortality
- Where severe anaemia is common, decreased maternal mortality and obstetrical complications

Benefits to all individuals:

- Improved fitness and work capacity
- Improved cognition
- Increased immunity
- Lower morbidity from infectious disease

Source: Modified from Stoltzfus, R. and Dreyfuss, M. **Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anaemia**, the International Nutritional Anaemia Consultative Group (INACG/WHO/UNICEF), 1998. Table 2, p. 2 (5).

Fortification of Foods with Iron

Background

Foods have been enriched with iron since the 1930s when it was added to cereal flour to replace iron lost during milling (29). Iron fortification refers to adding more of the nutrient than was originally in the food in order to combat iron deficiency. Iron is commonly added to foods, especially cereals and cereal products, in industrialized countries and in many countries of Latin America. It is being increasingly adopted in the Middle East and North Africa and in some Asian countries. Interest in iron fortification continues to grow in all regions. According to one analysis, where populations are at risk of iron deficiency, the fortification of cereals with iron yields US$84 in gained productivity for every US$1.00 spent (11).

Rationale for fortification

Fortification requires the identification of commonly eaten foods that can act as vehicles for one or more micronutrients and lend themselves to centralized processing on an economical scale. For the large and expanding populations of all socioeconomic classes that regularly purchase and consume commercially processed foods, fortification can make an important nutritional difference and offers a number of strategic advantages.

When superimposed on existing food patterns, fortification may not necessitate changes in the customary diet of the population and does not call for individual compliance; it can be dovetailed into existing food production and distribution systems. For these reasons, fortification can often be implemented and yield results quickly, and be sustained over a long period of time. It can thus be the most cost-effective means of overcoming micronutrient malnutrition.

By building on existing food production and distribution infrastructure, fortification engages the market system and the private food sector to tackle a public health problem. Industry provides much of the initial investment and the ultimate financing is borne by consumers. The private sector also offers technical expertise in production and marketing, and most important, a business-like approach to solving problems.

The role of governments in fortification programmes is mostly confined to advocacy, communication, setting standards, regulation, monitoring, and periodic evaluation. This can enable governments to concentrate the balance of their budgets on ensuring effective supplement delivery and dietary education to vulnerable groups, and to remote and disadvantaged populations.

Fortification reaches broad populations at minimal cost. The cost of addition of iron, either singly or with other micronutrients such as folic acid, B-vitamins, calcium, and even vitamin A, is a very small percentage of the cost of the flour: the cost of iron-folic acid fortification of wheat flour is less than US$0.36 for a ton of flour or US$0.04/kg. In food processing industries all over the world, the addition of conditioners, preservatives, vitamins, and minerals is not new.

In many cases, the equipment needed for fortification is already integrated into the process flow. The required investment in fortification technology is minimal and can often easily be absorbed by the producer. Ongoing costs of fortificant, marketing and quality assurance are usually absorbed in the normal market fluctuations for most foods. Incremental costs, often as low as 1-2 per cent of the commodity cost, are either passed along to the consumer or simply absorbed by the producer.

Fortification, when integrated into the food processing and distribution system, can become a permanent feature that can be sustained with little external support or investment.

In addition to the fortification of staple foods intended for general use, many foods for infants and young children, especially milk and cereal-based foods, are widely fortified. In the 1970s, FAO/WHO, the U.S. National Research Council and the European Society of Paediatric Gastroenterology and Nutrition (ESPGAN) Committee on Nutrition were among those bodies that set standards for fortifying infant formula and

complementary foods with iron and other micronutrients (11). Such foods have been shown to improve or maintain the iron status of young children. School meals can also be effective for delivering fortified products (29).

Several useful documents and guidelines have been developed to support fortification (see Annex I) and there have been a number of recent consultations and research studies dealing with specific issues related to the process.

Selection of suitable vehicles

General criteria for the selection of food vehicles suitable for micronutrient fortification are outlined in *Micronutrient Fortification of Foods: Current Practices, Research and Opportunities*, published by the Micronutrient Initiative (7), and include the following points:

Consumption

- High proportion of the population covered
- Regular consumption in relatively constant quantities
- Minimal variation in consumption patterns among individuals
- Appropriate serving size to meet a significant part of daily requirements of the micronutrient(s) added
- Consumption not related to socioeconomic status
- Low potential for excessive intake
- No change in consumer acceptability after fortification
- No change in quality as a result of fortification

Processing/storage

- Centralized processing
- Simple, low cost technology needed to add fortificant
- Good masking qualities
- High stability and bioavailability of added micronutrient(s) in final product
- Minimal segregation of the fortificant and food vehicle
- Good stability and storage

Wheat flour and maize meal are two major food vehicles that can be appropriately fortified with iron for much of the developing world. For wheat, iron is most often added in an amount that restores the iron lost during milling (milling removes about two-thirds of the natural iron content of a cereal), or to enrich the flour. Standards for fortification levels vary in different countries. For example, some levels of ferrous sulphate used to fortify wheat flour are: Canada 29-43 parts per million (PPM), Chile 30 PPM, Nigeria 35 PPM, Denmark 30 PPM, and the USA 44 PPM (7).

New research, particularly the demonstration of the impact of iron fortification of flour on the reduction of anaemia in Venezuela (42), has sparked a greater interest in flour fortification as one of the primary interventions needed to prevent iron deficiency in national populations.

The World Food Programme (WFP) now supplies iron-fortified flour in its programmes throughout the world. It has reached an agreement with UNICEF by which countries receiving unprocessed wheat can be assisted in setting up the necessary fortification equipment and receive iron fortificant for use at national mills.

Wheat flour, maize meal, infant cereals, infant formulas, and several high-energy foods packaged for feeding refugee groups and supplementing the nutrition of school children are currently fortified with iron on broad commercial bases. Salt, sugar, soy sauce, fish sauce, curry powder, milk powder, coffee, and other condiments have been successfully fortified in pilot studies.

Several recent international meetings on the control and prevention of iron deficiency have discussed the potential for recommending that all wheat flour be fortified in large parts of the world. Particular reference has been made to countries in the Eastern Mediterranean and Middle East regions (43), Central and Eastern Europe, and those of the Commonwealth of Independent States. Most of these countries have wheat flour as a widely used staple food and most milling is done in large, centralized mills.

A recent meeting reviewed rice fortification technologies and various aspects of a national rice fortification programme.[†] It was reported that fortified rice is a potential carrier of both iron and vitamin A, but that continuing research and advocacy are required to overcome existing constraints. Rinse-resistant rice grain premixes were reported to be an economical and effective means of delivering micronutrients in rice consuming areas. The challenge, however, is to deal with the logistical constraints of marketing rice fortified in this manner. Trials with double fortified (iron-iodine) salt in India and Ghana show promise and need more active follow-up and additional field trials. Sugar fortified with both vitamin A and iron-EDTA was successful in Guatemala (44).

Selection of an iron fortificant

Iron fortification has been shown to be effective in raising mean haemoglobin levels of study populations and producing shifts in the distribution curves of a population's iron status. Among the programme-relevant issues is an urgent need for international guidelines on the forms of iron that can be used as fortificants. Several authors have reviewed the merits of the various fortificants available and in use, and noted their advantages and disadvantages with respect to safety, affordability, stability, bioavailability, reactivity with other compounds, and efficacy in improving iron status. This issue is particularly

† International Workshop on Micronutrient Enhancement of Rice held in Stuttgart, Arkansas, USA in October 1998, organized by USAID and MI.

relevant in cereals with high phytate content where absorption of conventional iron compounds is quite low.

Several iron compounds have been used to fortify foods based mainly on evaluation of their reactions between the specific iron compound, the components of the food they fortify, and other micronutrients that may be added to the fortificant mix. The Micronutrient Initiative will make available publications that provide information on various fortification premixes and sources (45).

Bioavailability of the selected iron compound should be a key factor for deciding on fortificants. For example, because it is inert, ferric pyrophosphate has been widely used to fortify cereals, pasta products, and milk powder, and in suspension in liquid foods, such as cocoa drinks. Unfortunately, its absorption is extremely poor.

- Ferrous sulphate is an excellent, low-cost source of bioavailable iron but is inhibited by phytates and tannins. Its shelf life is limited to about six months in bulk cereals depending on ambient conditions. This chemical reacts with and causes colour and taste changes in some foods after long storage periods.

- Ferrous fumarate is used to fortify complementary foods of young children, such as biscuits and wafers (25). It is now used in Venezuela for the iron fortification of both wheat and corn bread (arepas). This compound is relatively expensive.

- Ferrous lactate is hygroscopic and cannot be used in dry foods, but is the preferred iron fortificant for ultra high temperature (UHT) milk and liquid formula diets (29). Liquid formulas have also been successfully fortified with BisGlycine iron chelate and with microencapsulated ferrous sulfate. Iron chelate is expensive.

- Elemental iron is widely used throughout Latin America and Asia. This compound needs to have a small particle size specified to ensure absorption. It is inexpensive.

New, emerging, and experimental iron fortificants

The potential uses of iron-EDTA (ethylenediaminetetraacetic acid) in food fortification programmes has been the subject of much attention and was recently reviewed by an "EDTA Task Force" meeting in Atlanta, GA, USA. It is two to three times more available in high-phytate meals than ferrous sulphate. It is more available than any other non-haem iron fortificant, actually improves the availability of non-haem iron in the diet,[†] and can also increase zinc absorption.

At a 1994 meeting on iron deficiency in London, this group also suggested that securing GRAS status (Generally Recognized as Safe) for iron-EDTA in whole wheat flour in the U.S. would help promote the use of iron-EDTA in other countries.[††] The production of adequate commercial quantities of food grade iron-EDTA at reasonable prices for use in fortification programmes was noted as an important issue.

The EDTA Task Force also discussed other compounds that affect the bioavailablity of iron. With regard to other enhancers, there is a need for more information on safety, functionality, and iron bioavailability while using heat-stable ascorbic acid added to cereals. In addition, the effectiveness, stability, cost, and effects on quality of fungal phytase added to whole wheat flour and corn meal to improve iron absorption should be studied.

Ascorbic acid increases the absorption of iron from all iron compounds, and unlike iron-EDTA, it also works in the presence of tea. Problems with adding ascorbic acid to foods as a fortificant are its poor stability during cooking and the need for expensive packaging of products that include this product because of its relatively poor stability.

There is currently considerable research being conducted aimed at phytate manipulation through such practices as soaking and/or fermenting cereals before, or as part of, the process of preparing them in prepared foods. However, at least 50 per cent of the phytate must be removed in order to improve iron absorption significantly. A combined process whereby ascorbic acid is added to counter the effect of phytates in iron absorption may reduce the need to remove most of the phytate.

Fortification safety

An issue often raised is the degree of risk of staple foods fortified with iron precipitating iron overload among persons susceptible to this condition. The MI/UNICEF document, *Major Issues in the Control of Iron Deficiency*, echoes the conclusion of several other research reports and national policy documents that the amount of iron likely to be ingested through fortification of staple foods, while enough to improve iron deficiency at the population level, is too small to pose significant risk, even to persons homozygous for haemochromatosis. The MI/UNICEF report notes that the possibility that certain individuals may at some time develop iron overload is a risk-benefit question. It concludes:

> *First: Iron fortification will not lead to the development of iron overload in normal individuals. This is because there is a very efficient system of down-regulation of dietary iron*

† While there are few doubts about the suitability of iron-EDTA iron, the group in Atlanta agreed that it would be useful to establish the conditions or situations in which iron-EDTA could be used in preference to adding iron alone. They also agreed that additional information is desirable on the effect of iron-EDTA, and related compounds on the bioavailabilty, stability, shelf life, quality, and baking properties of cereal products, such as whole wheat flour, corn masa, whole corn meal, and soy-cereal blends used as complementary foods.

†† At present no industrialized country fortifies cereal flour with iron-EDTA for human consumption, nor are there major production facilities for producing this product at the standards necessary. Developing country officials continually lament these facts when the potential benefits of selecting iron-EDTA as a cereal fortificant are discussed. A project has been proposed for the large-scale production of iron-EDTA to fortify soy sauce in China. Workshop participants agreed that this project should be systematically documented and monitored, and the results widely disseminated.

absorption and an actual blocking, at certain iron-store thresholds. This applies even to diets with high iron bioavailablility, high haem-iron content, and to iron fortified diets.

***Second:** Several genetic conditions predispose risk of iron overload. The risk has been found to be related to a defective gene when it is homozygous. This risk occurs among a small minority, mainly of European extraction, and largely concentrated in genetic "hot spots," not evenly distributed throughout the population. Heterozygotes, who are more numerous, are not at risk of iron overload.*

***Third:** The amount of iron added to the diet through fortification can make a significant rightward shift in the distribution of iron status of an iron-deficient population and fewer people become anaemic. However, such amounts would make little or no difference to the outcome for those with various haemoglobinopathies* (4).

Addition of other micronutrients along with iron in fortified foods

Many countries already fortifying staple food with iron are interested in including additional nutrients that may be useful in addressing other deficiencies at the population level. Once the logistic and financial problems of fortifying cereal products with iron are overcome, the costs of adding other nutrients are relatively small, so that adding them, even where there is a smaller health risk, is justified by the benefit. Folic acid is already included with iron in wheat flour in several countries. At least nine Central American and Caribbean countries, and five South American countries already add thiamin, riboflavin, and niacin, as well as folic acid with their iron fortification of cereals (46). There is interest in including vitamin A, B vitamins, calcium, and zinc in wheat and corn flour in a number of countries. The efficacy of an encapsulated iron-vitamin A-zinc mix that can be sprinkled over complementary foods or cooked foods is being evaluated in Nicaragua. This is more akin to supplementation than fortification but serves the same purpose.

Consensus Statements

1. Iron fortification of basic foods has been shown to be effective in reducing the prevalence of iron deficiency anaemia. This practice is well established in many countries, many of the relevant technologies are well known and it is both low cost and highly cost effective.

2. Food fortification with iron should be used much more extensively throughout the developing world. The expansion and acceleration of iron fortification of cereal flours will require a major advocacy effort by governments, international and bilateral agencies, and NGOs. The milling industry must be involved in this process. Agencies, NGOs, and programmes providing support for iron fortification should collaborate closely in the development of needed advocacy materials and in providing backup technical support.

3. More systematic efforts are needed to increase the sharing of information among countries with well-established fortification programmes and others not yet using this public health intervention in a widespread manner. International agencies, NGOs, and projects working to improve micronutrient nutrition should support greater advocacy, information sharing, and technical assistance in the area of iron fortification of basic foods.

4. Much greater efforts should be made to initiate or strengthen policies and mechanisms that result in iron fortification of complementary and other foods that are common in the diets of children. Among other actions, agencies should promote consumption of iron-fortified foods in the timely and appropriate complementary feeding of breastfed children.†

5. Standardized guidelines are needed for the selection of vehicles and fortificants for iron fortification programmes. The choice of an appropriate, cost-effective vehicle and fortificant is situation-specific. There are several excellent guidelines for selecting fortificants to assist nutrition and health professionals and others involved in the consideration of programmes to fortify staple or other foods with iron. These should be combined with the most recent information and experience and synthesized into a new *International Guide to Selecting Appropriate Vehicles and Iron Compounds for Food Fortification Programmes*. This task requires agreement among WHO, FAO, UNICEF, MI, and INACG. It should include a roster of experts and institutions that can provide advice or onsite consultation. Such a guide should be distributed widely through international and bilateral agencies as soon as possible.

6. Iron-EDTA is a fortificant that works well in the presence of high levels of phytate inhibitors. At the present time, recommendations for the use of iron-EDTA have been unnecessarily limited by its lack of GRAS (Generally Recommended As Safe) status, by the limited availability, and high cost of "food grade" iron-EDTA. If demand were established, large-scale, low-cost production of iron-EDTA for food use would not be a limitation.

7. Iron fortificants should, at minimum, have added folic acid in recommended quantities. There is evidence that the inclusion of zinc may be of benefit at negligible cost. The addition of thiamin, riboflavin, niacin, and calcium, as in many industrialized countries and Latin American countries, can benefit nearly all countries. Other nutrients such as vitamin A and ascorbic acid may be appropriate, depending on the vehicle and circumstances.

† There is no intention here to imply that infant formula, including fortified infant formula, should be substituted for breastmilk; the Technical Workshop emphasized the opposite.

8. Fortification with iron (and other micronutrients) in food aid and targeted feeding programmes is underutilized and applications to the fortification of foods for specific groups, both offsite (complementary foods, refugee rations, etc.) and onsite (preschool and school meals, etc.) should be expanded with a goal of making iron fortification a standard practice. Improved guidelines for identifying opportunities for effective fortification should be developed.

9. The provision of micronutrients is particularly important for the beneficiaries of food aid programmes, e.g., for refugees, displaced persons, and disaster victims. Agencies and donors involved in food assistance should provide commodities fortified with iron and other micronutrients to the extent possible and feasible, either through requesting donors to supply fortified commodities or through procurement of appropriately fortified foods.

10. Particular attention is required to the development of a sustainable local infrastructure for fortification including the equipment needed at mills to add fortificants and assure quality control of fortified foods.

11. Where practical, fortification programmes should include the use of small-scale facilities, despite the greater logistic difficulties.

SECTION 7

Use of Oral Iron Supplements

Background

While fortification of staple foods with iron can improve iron nutrition and play a major role in preventing iron deficiency, even for those populations who have access to and consume iron enriched foods, specific groups of persons are likely to need oral iron supplements to prevent and control iron deficiency and iron deficiency anaemia. With effective compliance among vulnerable groups in their routine use during specific periods of the life cycle, oral iron supplements can be an effective intervention in the integrated approach to preventing iron deficiency and iron deficiency anaemia.

The past focus of many anaemia interventions and international support for these interventions has been on daily oral supplementation of pregnant women with tablets containing ferrous sulphate and folic acid. Major organizations, including INACG, WHO, and UNICEF, now recommend routine iron supplementation of young children, adolescents, women of childbearing age, and pregnant women when the levels of anaemia in a population are more than 40 per cent (5).

The INACG/WHO/UNICEF (1998) guidelines help in determining the need for iron supplementation in these groups and in planning and implementing iron supplementation programmes. Additional guidance for programme planners can be found in several sections of the MI/UNICEF publication, "Major Issues in the Control of Iron Deficiency." Iron supplementation is further reinforced by technical consensus by INACG, WHO, UNICEF, and other groups, that the presence of endemic malaria should not limit the use of iron supplements to control iron deficiency anaemia (see Section 9).

The planning necessary to move from guidelines to effective iron supplementation programmes in the field should not be underestimated (see Figure 5).

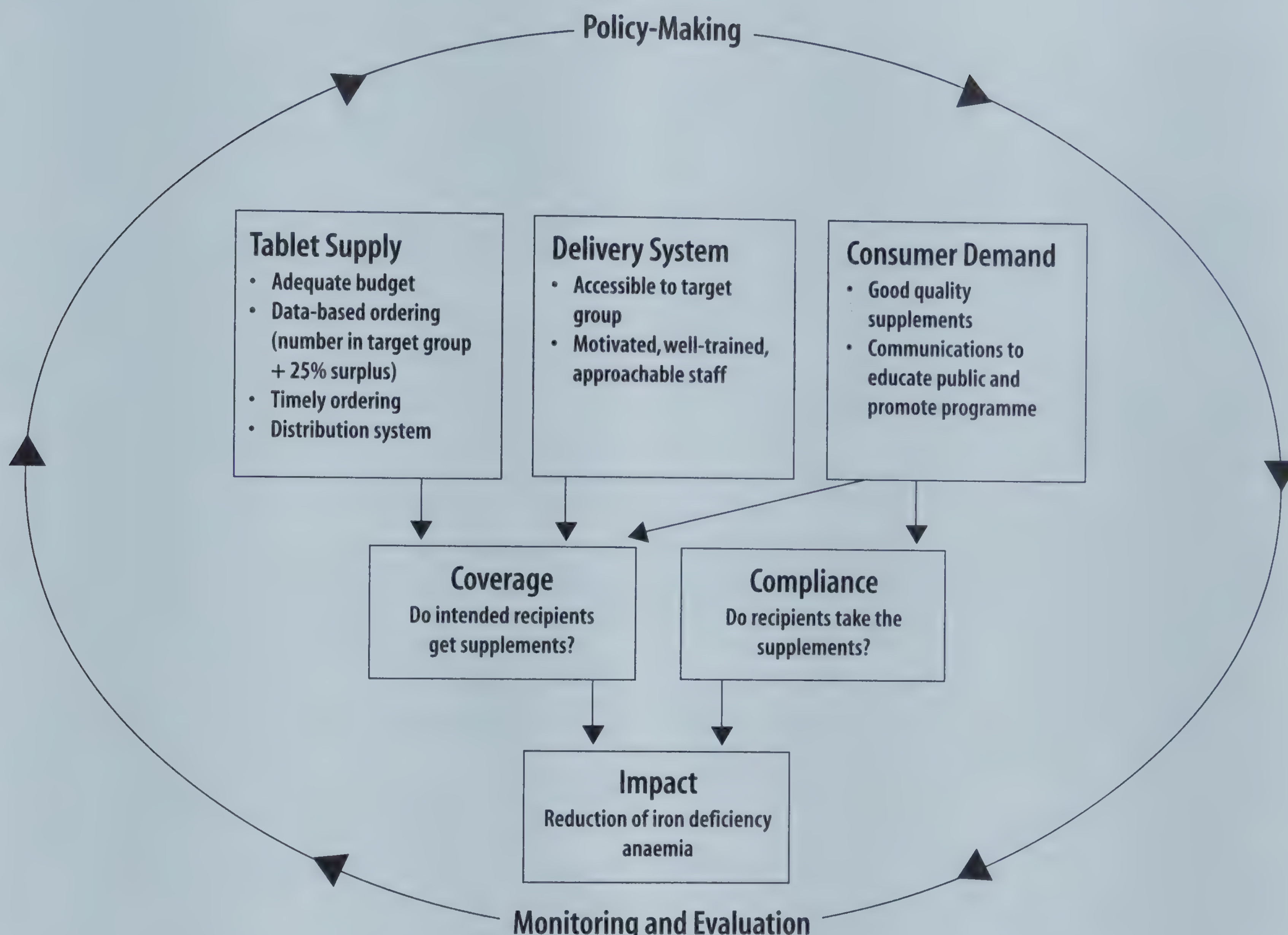
Many specialists agree that there is still no clear framework for assuring an effective iron supplementation programme. Iron supplementation, in the past, has often been conceived as a simple therapy for controlling anaemia in pregnant women and for treating anaemia in other groups, including young children. Even in these contexts, studies of compliance have found low levels of compliance where taking the iron tablets was unsupervised. Issues related to iron supplementation on which technical consensus has been sought include:

- the potential effectiveness of iron supplementation in large field programmes where populations are expected to comply with the use of supplements on a routine, unsupervised basis;
- the relative efficacy and potential effectiveness of daily, biweekly and weekly supplementation doses in programmes aimed at preventing iron deficiency anaemia;
- the levels and types of evidence, and other factors including cost differences, needed for WHO, UNICEF, and other organizations to recommend an intermittent supplementation dose as a programme option in large-scale interventions with various groups; and
- the safety and effectiveness of iron supplementation of pregnant women in malaria endemic areas.

Key factors affecting the effectiveness of iron supplementation programmes

Despite virtual universal acceptance of the efficacy and potential effectiveness of routine oral iron supplementation as a public health intervention to prevent iron deficiency, there are no documented instances of large-scale voluntary iron supplementation programmes significantly reducing levels of iron deficiency anaemia in a population. The continued and growing commitment toward iron supplementation within large organizations, such as UNICEF and WHO and many specialized groups and public health services around the world, appears to be based on confidence in the efficacy of an oral supplement to provide sufficient iron for most threatened groups, an assumption that supplementation programmes can

Figure 5: Elements of Successful Iron Supplemental Programmes



Source: Stoltzfus, R., Dreyfuss, M. Guidelines for the Use of Iron Supplements to Prevent and Treat Iron Deficiency Anaemia. 1998. The International Nutritional Anaemia Consultative Group (INACG), the World Health Organization (WHO), and the United Nations Children's Fund (UNICEF), Washington, D.C. USA. p. 18 (5).

be developed to overcome the known problems related to compliance, and that they will succeed in effectively reducing iron deficiency and iron deficiency anaemia levels in targeted population groups.

There are several types of factors related to iron supplementation programme success. Programme planners, leaders, and those developing monitoring and evaluation procedures are urged to assess and develop strategies that address these factors.

One category of factors affecting the effectiveness of supplementation programmes for all groups is related to widespread distribution and access to supplement supplies. A second set of factors affects individual voluntary compliance in taking/giving the supplements according to programme protocols. A third category relates to the organization of training and education as well as the development of communication strategies. Other important factors include the degree of community participation in and ownership of the programmes, intersectoral collaboration, and the strength of linkages to other health and nutrition programmes including other iron nutrition related interventions such as food fortification.

Assurance of effective supplementation in unsupervised settings is lacking

Programme specialists note the importance of understanding the complexity of planning and implementing an effective iron supplementation programme. Many factors make iron supplementation far more complex than, for example, supervised administration of vitamin A capsules every six months. The fact that iron tablets are an inexpensive and commonly used essential drug, long used at the primary care level with pregnant women, should not lead programme planners to assume that adding additional target groups and building high levels of compliance are simple matters.

While many factors identified as negatively affecting compliance (47) are related to distribution and/or access to iron tablets, there are also documented cases where intended recipients have been reluctant to take supplements on a regular basis, even when there are no supply interruptions and stocks of supplements are adequate at all antenatal sites. Poor individual compliance has also been attributed to complaints of gastrointestinal distress associated the iron/folic acid supplements, although some observers believe that the importance of this factor has been overstated with iron dosages now being recommended for routine use for adults. Discomfort with iron supplementation is generally mild and often disappears after one to two weeks. Dark stools are sometimes cited as a deterrent. Studies have also identified lack of counseling of women about the importance of good iron status, women's fear of having a large foetus and difficulties in delivery, and dissatisfaction with the appearance or taste of tablets as determinants of poor compliance (48).

In some trials, social marketing and other communications activities, sometimes combined with improved packaging of tablets, have resulted in improved compliance. In all cases a solid information component stressing education and counseling of the participating and target populations is required (5, 41). Integration of supplementation into a multi-intervention package is also important.

The efficacy of iron supplementation in raising haemoglobin levels in vulnerable groups, especially among anaemic individuals, when taken in established doses on a daily basis is well established in experimental settings. In the last few years a number of trials have been conducted on the efficacy of weekly dose protocols (49). Preliminary findings from a recently completed cross-analysis of studies of weekly and daily dose iron supplementation show that weekly doses of iron supplements were similarly or only slightly less efficacious compared with daily doses in improving haemoglobin and serum ferritin levels. However, the analyses also suggest that in only a few of the studies was either daily or intermittent iron administration completely effective in controlling anaemia (50).

Monitored interventions with daily iron have been shown to be very efficacious. However, once the monitoring was removed, daily dosing was, by and large, ineffective. Given the lack of definitive evidence and the known difficulties in achieving high levels of compliance in programmes calling for routine iron supplementation on a daily basis, debate is active regarding the effectiveness of either daily or weekly iron supplementation in large-scale programmes. It is hoped that unmonitored weekly dosing can be effective, but there is no proof of this as yet.

Iron supplementation to prevent and control iron deficiency in pregnant women

Anaemia rates in pregnancy exceed 40 per cent in most developing countries and constitute a significant public health risk in many industrialized countries as well. Most countries have policies of universal iron supplementation for women who use antenatal services or who are found to be anaemic during pregnancy. However, as a single intervention in developing countries to address anaemia in pregnancy in both its moderate and severe forms, supplementation alone has proven disappointing in terms of both process and impact, and its effectiveness has repeatedly been questioned. Nonetheless, in controlled situations where compliance is high, daily supplementation has been shown to be effective in improving or maintaining haemoglobin levels if started early enough in pregnancy.

In an effort to improve the effectiveness of anaemia prevention and control, INACG, WHO, and UNICEF recently prepared guidelines for iron supplementation for pregnant women as a step forward in reaching a practical consensus on iron supplementation protocols. These guidelines recommend daily supplementation of 60 mg elemental iron and 400 μg folic acid (normally contained in one 200 mg ferrous sulphate plus folic acid tablet) for six months during pregnancy and three months postpartum (5). Many experts agree that 30 mg of elemental iron per day is as likely to be as effective as 60 mg per day when taken on a regular basis throughout pregnancy. However, there is concern about the adequacy of even 60 mg per day in bringing women who do not take supplements for the full second and third trimesters to an adequate iron status before and after they give birth.

The INACG/WHO/UNICEF guidelines call for women who do not begin taking supplements at the beginning of the second trimester and continue them throughout pregnancy to continue with a 60 mg daily dose for six months postpartum, or take an increased dose of 120 mg daily during pregnancy (5).

There is growing consensus for more aggressive alternative strategies that aim toward preventing iron deficiency and iron deficiency anaemia throughout a full life cycle. The reduction of the prevalence of iron deficiency anaemia in pregnancy requires prevention strategies of ongoing routine supplementation that aim toward having women enter pregnancy with good iron stores, and assure that the women have an adequate dosage of supplements throughout pregnancy and postpartum.†

Research shows that neural tube defects, especially spinal bifida and anencephalia, in the developing foetus have a causal relationship with folic acid deficiency in the pregnant mother, and occur during the first 25 days of pregnancy. Because folic acid is usually combined with iron in a single tablet, the use of folic acid supplements to prevent neural tube defects can only be effective if they prevent folate deficiency during the first few weeks of pregnancy, a time when few women are aware of their pregnancy or seek antenatal services. Therefore, to reduce neural tube defects in the foetus, programmes should aim at preventing women from entering pregnancy in a folate deficient state. In practical terms, women should take ferrous

† Due to the breakdown of red blood cells acquired during pregnancy, haemoglobin levels and indicators of iron status tend to be misleadingly high during the first three postpartum months, obscuring the state of iron depletion that usually exists.

sulphate and folic acid supplements routinely during periods of life when becoming pregnant is possible, as well as throughout their pregnancy and/or consume foods fortified with iron and folic acid.

Breastfeeding plays a significant role in preventing iron deficiency in both infants and their mothers. Breastmilk, while not high in iron content, has iron that is highly bioavailable for the infant. For the mother, iron secretion into breastmilk does not constitute a substantial iron drain to the mother, and breastmilk iron content is not affected by maternal iron status. In addition because lactation delays the onset of menstruation and menstrual blood loss, breastfeeding helps protect maternal iron stores.

In some regions, maternal depletion of folic acid may occur during lactation, a situation that can be prevented by continuing the 400 μg of folic acid contained in most iron/folic acid supplements during the first six months postpartum.

Recent evidence suggests that vitamin A supplementation during pregnancy can reduce the risk of maternal mortality and improve haemoglobin response to iron in vitamin A deficient individuals (51).

For this reason, as well as evidence that addressing other micronutrient deficiencies in pregnancy can have significant benefits for both the mother and the infant, many countries are interested in including other nutrients in iron/folic acid supplements. Several trials of multiple-micronutrient supplementation in pregnancy are under way in developing countries and multiple-micronutrient supplements are widely used by pregnant women in industrialized countries.

Currently, national government recommendations for such supplements vary considerably among countries. International criteria are needed for recommendations on multiple-micronutrient additions to the current iron/folic acid supplement.

Iron supplementation to prevent and control iron deficiency in infants and preschool children

More than 22 countries have adopted public health policies calling for iron supplementation of infants and preschool children. It is anticipated that this number will grow quickly if the new INACG/WHO/UNICEF guidelines for iron supplementation are widely and effectively disseminated. This will also depend on stronger advocacy for programmes to prevent iron deficiency by major international and bilateral organizations concerned with public health and child rights, and on reducing costs associated with the prevention of this micronutrient deficiency.

Advocacy for such efforts will be reinforced by wider knowledge that anaemia in young childhood has serious and lasting consequences for cognitive development.

Breastfeeding remains a key to the health and nutrition of infants and young children. However, after six months, normal birth weight infants have used the iron stores they had at birth and breastmilk will not provide the amount needed as they continue to grow and develop rapidly. A number of recent consultations concluded that where iron-fortified cereals or other appropriate complementary foods are not available or widely consumed, iron deficiency anaemia in children aged six to 18 months is virtually certain to be an important public health problem.

With wide availability of affordable iron-fortified foods for children unlikely for some time in many countries, iron supplementation is a critical public health measure. As noted in the recent INACG/WHO/UNICEF guidelines, preventive iron supplementation is essential in this age group (5).

Of importance in achieving more widespread supplementation of children less than one year of age is improving the products available for this age group. Liquid iron supplements are costly to transport and store, and require packaging to enable caregivers to provide it in an effective, correct, and safe manner.

A USAID/OMNI/UNICEF consultation in 1996 suggested that a nutrient-fortified powder or "sprinkle" that can be mixed into complementary foods is promising, and such a product is now being tested in Nicaragua.

Supplementation programmes for infants and young children should include adequate information, education, and communication plans for promoting compliance and for improving the diets of children in order to lessen the need for supplementation. Evidence is accumulating that a multiple-micronutrient formulation may be useful in countries where children are prone to multiple deficiencies after the age of six months, even when they have been exclusively breastfed up to that time. However, there is as yet no agreement on what the composition of such a supplement might be.

Iron supplementation to prevent and control iron deficiency in school children and adolescents

In addition to addressing anaemia during pregnancy and children six to 18 months of age, public health services should implement policies that ensure the provision of adequate iron to nonpregnant women of childbearing age, young children, adolescents and, where indicated, school children (52). Too few national public health policies currently include this commitment. Stronger advocacy and considerable assistance are required to help with programme design and mobilizing resources for these wider, but desirable, efforts to prevent iron deficiency.

As previously noted, low stores of iron *before* pregnancy are the main determinants of iron deficiency anaemia in pregnancy, making it important that women have good iron stores throughout their childbearing years.

Adolescent girls, especially those not in school, and women who are not in regular contact with health or other services are hidden populations in many countries, and may be among the most difficult groups to reach on a regular basis. Well-designed strategies, often involving collaboration between health services and major workplaces for young women, community leaders and organizations, and communication channels that reach families, are important in providing access to iron supplements and encouraging compliance with supplementation protocols.

In addition, iron deficiency in adolescents, as well as in nonpregnant women, adversely affects their health, cognitive function, and ability to work. In some countries where school children have been found anaemic, iron supplementation has improved test performance.

There has been considerable recent discussion and debate about the potential for increased overall effectiveness and lowering costs through the use of a weekly dose of iron for public health programmes aimed at preventing iron deficiency in these groups. Trials have shown that weekly iron/folic acid supplementation can be efficacious in controlling anaemia if supplements are taken regularly (49).

It is important to emphasize that there is a lack of evidence that either daily or weekly iron supplementation in large programmes without supervision of compliance is sufficiently effective to significantly reduce or prevent anaemia in any group. Local compliance issues and cost factors have encouraged exploration of intermittent supplementation designs in a number of public health supplementation programmes aimed at anaemia prevention and control.[†]

Consensus Statements

General

1. The 1998 INACG/WHO/UNICEF Guidelines provide good guidance to policy makers and designers of supplementation interventions.

2. Lessons from existing programmes and trials on how to improve supplementation compliance by pregnant women should be considered in programme planning, monitoring, and process assessments. These lessons include:

   a. The importance of the infrastructure, training, and resources to maintain an uninterrupted supply of good quality iron supplements, including adequate attention to those factors necessary to allow women to comply with supplementation protocols. More specifically:

   - resources for procuring good quality supplements
   - supply logistics
   - distribution channels
   - access to service providers
   - training of all those involved in distribution

   b. Iron supplementation activities need to be integrated with antenatal care, promotion of breastfeeding, family planning and reproductive health, control of infectious diseases, and other primary health care services.

   c. Participation of family members and the community is important to ensure compliance with routine iron supplementation.

   d. It is essential to carry out well-planned process monitoring of supplementation compliance.

   e. The need and importance of supplements of good quality, attractively packaged, with an adequate shelf life must be recognized.

3. Each programme using, or planning to use, the standard ferrous sulphate and folic acid supplement should include an evaluation of the potential benefits relative to costs of adding additional micronutrients. Additional nutrients with the most potential to improve health and nutritional status include vitamin A, zinc, and riboflavin. A high prevalence of iron deficiency is frequently associated with zinc deficiency.

4. All programmes should include a strong component to monitor and assess its key processes and to evaluate its effectiveness. For those exploring weekly supplementation, monitoring of both efficacy and effectiveness are important because controversy about the potential of this approach continues. Experiences, whether positive or negative, should be reported nationally and to the international community.

5. All supplementation programmes require process and impact monitoring under large-scale conditions. Governments and international and bilateral agencies supporting supplementation programmes of any kind should include funds to support monitoring and the international reporting of results.

Iron supplementation during pregnancy and postpartum

1. Among all populations, including those in industrialized countries, a sizable percentage of women will become iron deficient during pregnancy unless they take iron supplements.

2. Routine daily iron supplementation during pregnancy is now an essential part of public health efforts to prevent and control iron deficiency anaemia, assure good maternal health during pregnancy and birth, and assure that infants begin life with good iron stores, until fortification approaches and/or pre-pregnancy supplementation succeed in raising to healthy levels the iron stores of women when they enter pregnancy.

3. The long term goal of iron deficiency anaemia control programmes should be to *prevent* iron deficiency in groups at risk including young children and women of childbear-

[†] Weekly supplementation is now national policy in Panama (girls in school), and Indonesia (for female factory workers). Small-scale programmes using a weekly supplementation protocol are underway in the Philippines and Vietnam. Weekly dosing with ferrous sulphate and folic acid, along with fortification of wheat flour and dietary education was selected as the protocol for integrated programmes to prevent and control iron deficiency anaemia among young children and women in five countries in Central Asia.

ing age, the latter to ensure that they do not enter pregnancy in an anaemic state. In developing countries, the majority of women do not have iron stores at levels needed to bring them through pregnancy without becoming iron deficient and are not able to maintain their stores when consuming only their usual diets.

4. Daily iron/folic acid supplementation in pregnancy according to the protocols recommended by INACG/WHO/UNICEF is a safe public health measure for women in all countries including those where HIV/AIDS and malaria are endemic. An analysis of controlled clinical trials of iron supplementation in malarious areas by an expert group, convened by INACG, concluded that available data from malaria-endemic regions indicate that the known benefits of iron supplementation outweigh any risk of exacerbating the malaria.

5. In areas where hookworm, and/or schistosomiasis are endemic, supplementation with ferrous sulphate and folic acid for pregnant women (and other population groups) is particularly important where iron deficiency is prevalent.

Supplementation of infants and young children

1. Iron supplementation programmes for infants and young children should have a high priority. The INACG/WHO/UNICEF guidelines provide criteria for giving such priority to the supplementation of young children with ferrous sulphate and folic acid:

   a. Where iron-fortified complementary foods are not widely or regularly consumed by young children, all infants should receive iron/folic acid supplements after six months of age.

   b. If the prevalence of anaemia is less than 40 per cent, the duration of supplementation should be from six months until 12 months of age for infants of normal birth weights, and from two months until 12 months for low birth weight infants (12.5 mg elemental iron plus 50 μg folic acid daily). If the prevalence is greater than 40 per cent, all children should be supplemented daily until 18 months of age.

   c. If the prevalence of anaemia in children is not known, the prevalence of anaemia in pregnant women should be taken as a proxy indicator.

2. It is important to accelerate the development of affordable, high-quality supplements for infants and young children that are too young to safely swallow pills.

3. Infants and young children at risk of iron deficiency anaemia are also at risk of impaired health, growth, immunity, and cognitive development. Consistent with their policies on child health, child development, and promotion of child rights, governments, UNICEF, WHO, and other agencies should increase their own priorities for policy advocacy and support of programmes that include iron supplementation and increase their work with countries to improve programme effectiveness.

Supplementation of school children, adolescent girls, and nonpregnant women

1. For populations with evidence of anaemia as a public health problem, oral iron supplementation of adolescents and women of childbearing age is recommended.

   a. Where anaemia prevalence exceeds 40 per cent in pregnant women, it can be presumed that universal supplementation of adolescent girls (at a minimum, those ages 12-16 years) and non-pregnant women of childbearing age is warranted.

   b. In any country, the presence of anaemia signals the existence of an iron deficiency problem justifying actions that include food fortification and other approaches that may fall outside of the health system.

2. Evidence is growing that in some situations weekly supplementation is efficacious in preventing anaemia when compliance is achieved. However, there is still a need to further assess its effectiveness under programme conditions. The lower cost of the dosage, lesser frequency of side effects, and the possibility of its promotion as a weekly "event" in communities, supported by communication activities make it attractive if it can be shown to be effective in practical programmes.

3. Where iron deficiency anaemia is a public health problem in school children, iron supplementation should be provided. This should be undertaken even if families must purchase their own iron tablets, a practice demonstrated successfully in trials based on weekly supplementation of school children and adolescent girls in northern Thailand.

Communication for Dietary Change

Background

There are many populations whose diets do not contain adequate available iron to meet physiological needs, particularly those of young children, women of childbearing age, and pregnant women. In diets that contain sufficient iron, most iron deficiency results from insufficient bioavailability or impaired absorption. Good sources of iron are well known, as are the major inhibitors and promoters of the absorption of non-haem iron. A recent review describes assessment tools for quantifying the bioavailability of iron in diets and predicting the impact of dietary modifications (37).

The extent of iron deficiency found in most developing and some industrialized countries' populations is ample evidence that their dietary practices are not adequate to ensure sufficient available iron. Dietary iron availability can be improved by better choice of food purchased, meal composition, cooking procedures, and distribution to family members. In some cases, particularly where substantial meals are taken outside the home, individuals can choose foods and meals providing good iron nutrition. Nevertheless, there has been no published evidence to date that programme interventions based mainly on conventional nutrition education have made a substantial difference in preventing or controlling iron deficiency on a population scale. Future efforts to improve iron status through dietary change should be based on analysis of what is feasible and affordable, and on the use of greatly improved communication strategies that aim toward specific behavioural objectives.

Involving communities in problem assessment and analysis enables people to understand dietary determinants of iron deficiency and identify opportunities to overcome dietary constraints in locally appropriate ways. Efforts should be made to avoid top-down educational approaches, in favour of more participatory approaches that allow women and mothers to strengthen their personal knowledge about, and commitment to, the behaviours needed.

A major challenge for communication strategies is to overcome the lack of motivation in meeting a threat to health that is most often not immediate or easily recognized. Iron deficiency is truly one of the "hidden hungers."

Information, education, and communication strategies aimed toward changing the food consumption behaviours of large and diverse populations should address the fact that many people have extremely limited resources and low levels of education. Improvement in the socioeconomic status of families is likely to increase intakes of foods that are iron-rich, particularly meat. In particular, women should be targeted by effective communications to help ensure that they use increased income for better quality and quantity of food.

Community-based communication has to be combined with advocacy at various governmental levels. Government policy decisions often influence community access to foods high in available iron. Agriculture, trade, and industry can make an important contribution to the availability and affordability of iron-rich foods. Increasing employment, equity, and appropriate research can all positively impact on nutrition, including iron status.

Consensus Statements

1. In order to develop effective communication and education strategies aimed at improving dietary behaviour, countries should use existing food intake and meal composition data to identify foods that are rich in absorbable iron. They must be accessible, affordable, and acceptable by a substantial proportion of the populations, including those in lower socioeconomic groups. This requires estimation of iron bioavailability. If such foods cannot be identified, this points to an even greater need for fortification of staples as a food-based strategy.
2. Efforts to improve dietary iron bioavailability through changing the consumption of enhancers and inhibitors of

iron absorption are worth encouraging even though they are not likely to improve iron status substantially when non-haem iron intakes are low. The latter is particularly likely to be true where the dietary staples are low in iron, e.g., unfortified white rice, white wheat flour, or maize meal. In general, the higher absorption of haem-iron (40 per cent of total iron in meats) from animal sources will not be affected by dietary enhancers and inhibitors and will improve the absorption of non-haem iron.

3. If effective sources of iron or ascorbic acid can be identified, they should be promoted to vulnerable population groups along with information about the adverse consequences of iron deficiency and anaemia.

4. Consumption of foods high in available iron, especially meats (beef, pork, lamb, fowl, fish, etc.) and liver is more likely to improve iron status than increasing ascorbic acid intakes or attempting to reduce the intake of tea with meals. This may not be economically feasible, although some animal products, such as liver, are both cheaper and higher in micronutrients including not only iron but also vitamin A, zinc, and B vitamins. Promotion of such products for use in diets of vulnerable groups, such as infants, young children, and pregnant and lactating women, may be an effective strategy for improving their iron status if promotional efforts take into account local circumstances and possibilities.

5. All iron interventions require a strong communication strategy with a plan for effective education and counseling by well-informed service providers who focus on specific actions that include:
   - complying with supplementation;
   - increasing consumer choice of fortified foods; and
   - preparation and consumption of meals providing greater iron intake and/or better absorption of iron.

   These activities should integrate actions and messages that lead to improved dietary behaviours overall as well as to the use and consumption of fortified food products and targeted iron supplements.

6. Strategies must use participatory approaches to develop locally relevant processes, channels, and messages that will promote better food choices and meal patterns that will in turn lead to greater intake and absorption of iron by family members vulnerable to iron deficiency.

7. Without fortification or supplementation, communication strategies for dietary behaviour change are unlikely to be adequate in themselves in either treating or preventing iron deficiency and anaemia. This is particularly so in populations characterized by poverty and diets that are poor in haem-iron and other essential nutrients. Poverty reduction, therefore, will be a key element of efforts to reduce micronutrient malnutrition. Where iron-rich food sources are available, or better dietary practices can enhance the absorption of iron, communication for dietary behaviour change is an important and sustainable part of any strategy to combat iron deficiency and anaemia.

SECTION 9

Public Health, Child Spacing, and Promotion of Breastfeeding:

Programme Linkages Supporting Prevention of Iron Deficiency

Background

Linkages between and among public health interventions are always important to improve cost-effectiveness of logistics, training, and service delivery systems, and to assure that the health and nutrition problems of individuals are treated in a holistic manner in all significant aspects of their lives and environments. Interventions to prevent iron deficiency should be integrated among themselves and also with other health-related programmes. These include, as priorities, control of maleria and helminths, particularly hookworm and schistosomiasis; programmes to improve maternal and reproductive health; breastfeeding promotion; and the new initiatives for Integrated Management of Childhood Illness (IMCI).

Intestinal helminths

Helminths can be an important cause of iron deficiency anaemia. A study of school children in Zanzibar found iron needs to be doubled because of blood loss due to hookworm disease (53). Hookworm intensity affects morbidity, growth, and school performance, and contributes significantly to iron deficiency and anaemia. In some populations haemoglobin status is linearly related to hookworm egg count in the stool. There are now inexpensive and effective drugs for controlling helminths and preventing blood loss from hookworm for up to 12 months.[†]

While no objective criteria currently exist (including in helminthic endemic areas) for initiating a helminth control programme, it is recommended in the INACG/WHO/UNICEF guidelines and some national plans that actions to address this type of infection be integrated into international anaemia control guidelines and national programmes for controlling iron deficiency (54). Behavioural changes, such as better faeces disposal and the wearing of shoes, can also help eliminate hookworm infection as a public health problem.

In Egypt and several other countries of that region, another helminth, *Schistosoma haemotobium*, contributes to iron deficiency through urinary blood loss. Like hookworm, it is controlled by a combination of behavioural change and antihelminthic treatment. *Schistosoma mansoni* infection can cause severe anaemia due to bleeding of intestinal nodules.

Deworming as an isolated programme is often difficult to promote and seldom has a high priority among health officials. It is believed that integrating helminth control into iron deficiency and iron deficiency anaemia prevention and control programmes can generate stronger support for such efforts (54). Similarly, antihelminth treatment has been integrated into the WHO/UNICEF Programme, Integrated Management of Childhood Illness (IMCI). While this programme addresses infants and young children, community level helminth control is extremely important for school age children as well.

Helminth treatment should be strongly linked to interventions that increase iron intakes, such as fortification and supplementation. Many of the constraints in logistics, operations, training, and community education aspects of helminth control are similar to those of oral iron supplementation. Likewise, operating these components in a synergistic manner makes good sense, particularly because of the causal relation of some helminth infections to anaemia.

The recent INACG/WHO/UNICEF supplementation guidelines include recommendations for intestinal parasite control complementary to iron supplementation for pregnant women, children 6–24 months and other population groups. They include a recommendation that where hookworms are

[†] For children over two years of age, where hookworms are the main parasites, the following drugs can be used: Albendazole (400 mg single dose), or Mebendazole (500 mg single dose or 100 mg doses two times a day for three days). In trichuris and ascaris transmission areas Mebendazole is preferred. Albendazole is not recommended for children under two years of age. Mebendazole is being recommended for children over two years of age by the WHO/UNICEF programme "Integrated Management of Childhood Illness."

endemic (prevalence more than 20 per cent), there should be universal antihelminthic treatment at least annually to children more than five years of age and adults as an important complement to supplementation and other programmes to reduce iron deficiency anaemia (5).

Malaria

Iron deficiency anaemia is prevalent in most areas of the world where malaria transmission is endemic. There has been concern expressed about the interactions between iron status and malarial infections that have, in some cases, constrained development of programmes to prevent and control iron deficiency anaemia. The general concern was about the safety of giving iron supplements to individuals where malaria was endemic. A 1998 INACG draft report reviewing the *Safety of Iron Supplementation Programmes in Malaria Endemic Regions* is summarized here (55).

The report identified nine published and four unpublished placebo-controlled trials of iron supplementation in malarious areas. The 13 trials ranged in sample size from 80 to 841, over 5,000 subjects with two in infants, four in preschool children, three in school age children, and four in adults with two in pregnant women. Eleven of the trials were carried out in Africa and two in Papua New Guinea (55). An analysis of all trials together found that iron supplementation did not increase in the risk of malaria attack with any statistical significance. However, it was noted that in most trials the case definitions used had low specificity that could result in underestimation of the relative risk. Iron supplementation did increase the risk for *Plasmodium falciparum* malaria. There was improvement in all trials where haemoglobin change was measured (55).

The INACG report made the following conclusion:

> *"Current international guidelines recommend the routine use of iron supplements for individuals living in communities at significant risk of iron deficiency (INACG/WHO/UNICEF, 1998). The available data from malaria endemic regions indicate that the known benefits of iron supplementation far outweigh the risk of adverse effects caused by malaria. The implication is therefore, that oral iron supplementation should continue to be recommended in malarious areas where iron deficiency anaemia is prevalent (55)."*

The major recommendations from that report were discussed and agreed on by participants at the Technical Workshop and form the basis of the consensus statements at the end of this section regarding iron supplementation of pregnant women and young children, especially infants of low birth weight, in malarial areas.

Maternal and reproductive health

There are several well-known linkages between prevention of iron deficiency and maternal and reproductive health. For example, new programmes aimed at reducing maternal mortality often include refresher training in obstetrics. This provides an excellent opportunity to reinforce proper delay in clamping the umbilical cord, which can significantly affect the iron stores of the infant (56).

In programmes promoting birth control, specific attention should be paid to the effect that various birth control methods may have on iron deficiency and its prevention. For example, many older types of intrauterine devices (IUDs) increase menstrual flow and thereby contribute to loss of iron. New IUDs with low release of progesteronal agents minimize this factor. Many brands of oral contraceptive pills include iron pills instead of the placebos often added to pill packets so that women do not break the monthly cycle of daily pills. More should be learned about the efficacy and effectiveness of this type of daily-intermittent iron supplementation on the prevention and control of iron deficiency.

Breastfeeding promotion

Breastfeeding promotion efforts including the Baby Friendly Hospital Initiative (BFHI) and programmes to prevent iron deficiency should be integrated as well. The high bioavailability of the iron in breastmilk and the importance of exclusive breastfeeding should be stressed both in programmes promoting breastfeeding and those aimed at preventing iron deficiency. The effect of lactation in delaying the onset of menstruation following birth provides women with a longer period during which they can build iron stores. This reinforces the need for promotion of prolonged breastfeeding and should be closely linked to programmes to prevent iron deficiency.

Cross-training between these breastfeeding and iron nutrition-related programmes is also important to ensure that low birth weight infants begin receiving iron supplements at two months of age, while normal birth weight infants receive iron supplements from six months of age. It is also necessary to stress that this micronutrient requirement is not related to the quality of breastmilk, and that iron supplementation of infants and women postpartum in no way reduces the desirability of exclusive breastfeeding for four to six months.

Where maternal depletion of folic acid during lactation is a problem, the INACG/WHO/UNICEF guidelines on use of iron supplements that include folic acid should be followed (5).

Integrated Management of Childhood Illness (IMCI)

Integrated Management of Childhood Illness (IMCI) projects are expanding rapidly in Africa and other regions. IMCI includes a training module developed by WHO on the "Treatment of Anaemia" in young children. This module calls for routine assessment for anaemia of all young children presented at health facilities for any illness and outlines treatment procedures. The country-level adaptation of this module needs to be linked to existing and planned efforts to prevent and control iron deficiency, to assure coordination and mutually supportive approaches. IMCI programmes integrate assessment and treatment procedures and enhance clinical training for primary care health professionals and preservice medical students. These activities offer important links to programmes

to prevent iron deficiency in young children. Close coordination is needed between those developing IMCI projects and those working to strengthen programmes to prevent and control iron deficiency and iron deficiency anaemia in young children.

Consensus Statements

1. The integration of helminth control into programmes for preventing and controlling anaemia should be supported. Deworming programmes can be linked to existing activities and service-delivery mechanisms and contribute to the control of iron deficiency. The proportion of anaemia caused by hookworm infection varies greatly with location. However, in countries where hookworm is endemic (prevalence more than 20 per cent), there should be universal anthelminth treatment at least annually, as a complement to supplementation and other programmes to reduce iron deficiency anaemia. Treatment with praziquantel is also recommended for areas where urinary schistosomiasis is endemic. To bolster support for hookworm and schistosomiasis control and prevention, professional advocacy is needed to highlight the impact of these helminths on morbidity and on nutritional status.

2. Birth spacing helps women to recover from pregnancy-related iron losses. This is particularly true if appropriate contraceptive methods are used since these reduce menstrual blood loss. In general, intrauterine devices (IUDs) increase menstrual flow, which, if accumulated across time, is equivalent to the blood loss associated with a pregnancy every three to four years.

3. Exclusive breastfeeding provides women with lactational amenorrhea, a natural form of birth spacing that allows time for iron stores to be built up prior to subsequent pregnancies. The iron in breastmilk is highly bioavailable and supplies adequate amounts for most exclusively breastfed infants of normal birth weight for the first six months of life. After six months of age, complementary feeding of iron-rich or iron-fortified foods or supplementation is necessary to meet iron requirements.

4. Prolonged breastfeeding also helps avoid the shift to cow's milk which is high in casein, calcium, and phosphates that inhibit iron absorption, thereby promoting iron deficiency. As noted in Section 7, in areas where iron deficiency anaemia is a significant public health problem, infants should receive iron supplements from six to 18 months of age (low birth weight infants from two months) as outlined in the INACG/WHO/UNICEF guidelines.

5. Programmes for the prevention of iron deficiency and iron deficiency anaemia should be well coordinated with IMCI projects that include a module for assessing and treating iron deficiency anaemia.

6. The benefit of delaying ligation of the umbilical cord until it stops pulsating can be detected by better iron status in early infancy.

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ANNEX I

Guidelines, Research, Reports, and Reference Materials Used in Preparing the Workshop and Report

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Groups and Organizations Providing Information, Documentation, Technical Assistance, and Resources

Canadian International Development Agency (CIDA)
200 Promenade Portage, Hull, Quebec, Canada K1A 0G4
Fax: (1 819) 953-5469; http://www.acdi-cida.gc.ca
CIDA supports micronutrient activities in Africa, Latin America, and Asia.

Caribbean Food and Nutrition Institute (CFNI)
University of the West Indies
P.O. Box 140, Kingston 7, Jamaica
Ph: (1 809) 927-1540 Fax: (1 809) 927-2657
CFNI improves food and nutrition situations in its member countries through education, training, information dissemination, coordination, and research.

Food and Agriculture Organization of the United Nations (FAO)
Viale delle Terme di Caracalla, 00100 Rome, Italy
Ph: (39 06) 57051 Fax: (39 06) 57053152
http://www.fao.org
FAO provides assistance and support to governments in developing the food, agriculture, and nutrition components of their micronutrient strategies.

German Agency for Technical Cooperation (GTZ)
P.O. Box 3852, Jakarta, 10038 Indonesia
Ph: (62 21) 324007; Fax: (62 21) 324070
http://www.gtz.de/laender/asp/index.asp
The GTZ office in Indonesia is actively involved in iron supplementation programmes. GTZ provides short-term and long-term technical assistance including programmes to build national capacities of nutrition researchers and commodity support for food fortification in selected countries.

Helen Keller International (HKI)
90 Washington St. 15th Floor, New York, NY 10006, USA
Ph: (1 212) 943-0890; Fax: (1 212) 943-1220
http://www.hki.org
HKI provides technical assistance on a wide range of components of micronutrient deficiency control programmes, including advocacy, assessment, training, social marketing, and operational research.

Instituto de Nutricion de Centro America y Panama (INCAP)
Centro Regional de Documentation, Apartado 1188, 01901, Guatemala City, Guatemala
Ph: (502) 471-5655; Fax: (502) 473-6529
http://www.incap.org.gt
INCAP promotes practical research and capacity building through training, formal education programmes, technical assistance, research, and information services.

International Life Sciences Institute (ILSI)
1126 16th St. NW, Washington, D.C. 20036, USA.
Ph: (1 202) 659-0074; Fax: (1 202) 659-3859
http://www.ilsi.org
ILSI is a nonprofit, worldwide foundation established in 1978 to advance the understanding of scientific issues related to nutrition, food safety, toxicology, and the environment. Headquartered in Washington, D.C., ILSI has branches in over 12 countries. ILSI encourages the development of a common standard by which scientific leaders can assess products, technologies, and public health strategies. ILSI houses the International Nutritional Anaemia Consultative Group (INACG).

International Nutritional Anemia Consultative Group (INACG)
ILSI Human Nutrition Institute
1126 16th St., NW, Washington, D.C. 20036, USA
Ph: (1 202) 659-0074; Fax: (1 202) 659-3859
http://www.ilsi.org/inacg.html
The International Nutritional Anemia Consultative Group (INACG) with funding from USAID, sponsors international meetings and scientific reviews and convenes task forces to analyze issues related to the aetiology, treatment, and prevention of nutritional anaemia. The outcome of these deliberations is then made available to policy makers and programme planners for their use.

Iron Deficiency Program Advisory Service (IDPAS)
International Nutrition Foundation
P.O. Box 500 Charles St. Station, Boston, MA 02114-0500, USA
Ph: (1 617) 227-8747; Fax: (1 617) 227-9405
E-mail: unucpo@zork.tiac.net
IDPAS is an INF project dedicated to accelerating and strengthening national programmes to prevent iron deficiency in developing countries and countries in transition. IDPAS provides senior advocacy support, rapid response to field personnel's technical questions, and collaborates to expand networks for sharing technical resources and research results on iron deficiency.

Linkages
Academy for Educational Development
1255 23rd St., NW, Suite 400, Washington, D.C. 20037, USA
Ph: (1 202) 884-8000; Fax: (1 202) 884-8400
http://www.aed.org/intl/health.html
Linkages is the principal USAID initiative for improving breastfeeding and related maternal and child dietary practices.

The Manoff Group
2001 S St., NW, Washington, D.C. 20009, USA
Fax: (1 202) 745-1961
http://ourworld.compuserve.com/homepages/manoffgroup
The Manoff Group provides technical assistance in social marketing in nutrition and health programmes, including micronutrient malnutrition.

The Micronutrient Initiative
c/o International Development Research Centre
P.O. Box 8500, 250 Albert St., Ottawa, Ontario, Canada K1G 3H9
Ph: (1 613) 236-6163, Fax: (1 613) 236-9579
http://www.micronutrient.org
The Micronutrient Initiative was established in 1992 as an international secretariat within IDRC in Canada by its principal sponsors: Canadian International Development Agency, International Development Research Centre, United Nations Children's Fund, United Nations Development Programme, and the World Bank. The mission of the MI is to provide the impetus to strengthen, expand, and accelerate operational programmes to achieve goals of the World Summit for Children.

MOST
International Science and Technology Institute (ISTI)
1820 N. Fort Myer Drive, Suite 600, Arlington, VA 22209, USA
Ph: (1 703) 807-0236; Fax: (1 703) 807-0278
MOST is a USAID flagship technical assistance project in the micronutrient arena. Its primary purpose is the improved and enhanced delivery of micronutrient interventions including supplementation, food fortification, and other food-based approaches. MOST is a cooperative agreement between USAID and the International Science and Technology Institute (ISTI). ISTI's partners include: JHU, HKI, AED, IFPRI, CARE, Save the Children, PATH, PSI, and IESC. Inquiries may be directed to Roy Miller, Project Director, at E-mail: Mrmiller@istiinc.com

MotherCare III
John Snow Inc.,1616 North Fort Myer Drive, 11th Floor, Arlington, VA 22209, USA
Ph: (1 703) 528-7474; Fax: (1 703) 528-7480
http://www.jsi.com/intl/mothercare
With funding from USAID, MotherCare works to improve pregnancy outcomes by strengthening and improving service delivery, influencing behaviours that affect the health and nutritional status of women and infants, and enhancing policy formulation at the regional and national level for maternal and neonatal health care.

Pan American Health Organization (PAHO)
525 Twenty-third St., NW, Washington, D.C. 20037-2895, USA
Ph: (1 202) 974-3000; Fax: (1 202) 974-3663
http://www.paho.org
PAHO, a regional office for the World Health Organization, provides technical assistance to countries in the Americas for iron deficiency anaemia control programmes.

The Partnership for Child Health Care (BASICS)
1600 Wilson Boulevard, Suite 300, Arlington, VA 22209, USA
Ph: (1 703) 312-6800; Fax: (1 703) 312-6900
http://www.basics.org
This partnership manages the USAID-funded BASICS project. The goal of BASICS is to continue and sustain reductions in morbidity and mortality in infants and children in developing countries.

Program Against Micronutrient Malnutrition (PAMM)
Department of International Health, 720 Grace C Rollins Building, Rollins School of Public Health of Emory University, 1518 Clifton Road NE., Atlanta, GA 30322, USA
Ph: (1-404) 727-4553; Fax: (1 404) 727-4590

E-mail: gmaberl@sph.emory.edu
http://www.emory.edu/GCA/healthcare.pamm.html
PAMM is a collaborative effort of the Rollins School of Public Health, CDC, and the Carter Center designed to completely eliminate micronutrient malnutrition around the world. PAMM holds training courses on laboratory methods and communication and management aspects of micronutrient control programmes.

Program for Appropriate Technology in Health (PATH)
4 Nickerson St., Seattle, WA 98109, USA
Ph: (1 206) 285-3500; Fax: (1 206) 285-6619
http://www.path.org
PATH identifies, develops, and applies appropriate and innovative solutions to public health problems including micronutrient malnutrition.

Project SUSTAIN
National Cooperative Business Association, 1400 16th St., NW, Box 25, Washington, D.C. 20036, USA
http://www.cooperative.org
Project SUSTAIN (USAID-funded) provides access to the U.S. food processing and marketing industry for small and medium-sized food processing companies, host government officials, and USAID missions in developing countries.

Swedish International Development Agency (SIDA)
International Child Health Unit, Uppsala University 75185, Uppsala, Sweden
Ph: (20 08) 698-5000; Fax: (20 08) 208864
http://www.sida.se
SIDA is a bilateral agency that supports nutrition initiatives in anaemia through capacity building and institution building activities.

UN Administrative Committee on Coordination/Sub Committee on Nutrition (ACC/SCN)
c/o World Health Organization, Avenue Appia 20, CH-1211 Geneva 27, Switzerland (The ACC/SCN has a new visiting address at No. 5, Route de Morillons, Geneva)
Ph: (41 22) 791-0456; Fax: (41 22) 798-8891
http://www.unsystem.org/accscn
The SCN serves as a focal point for harmonizing and disseminating information on nutrition policies and activities in the UN system.

UNICEF
3 UN Plaza, New York, NY 10017, USA
Ph: (1 212) 326-7000; Fax: (1 212) 887-7465
http://www.unicef.org
Through its Country, Area Offices and Regional Offices and the Nutrition Section of its Headquarters, UNICEF provides financial and technical support for developing country activities aimed at controlling micronutrient deficiencies through supplementation, fortification, and dietary modification. (UNICEF Supply Division is listed separately)

UNICEF Supply Division
2100 Copenhagen OE, Denmark
Ph: (4535) 273 527; Fax: (4535) 269 421
UNICEF Supply Division provides procurement services for fortification dosing equipment, fortificants, and supplements. Training and AV equipment, laboratory equipment, and many other commodities used in programmes and for capacity building can be procured through the UNICEF Supply Division.

US Agency for International Development (USAID)
Office of Health and Nutrition, Bureau for Global Programs, Field Support and Research
Washington, D.C. 20523- 1917, USA
Ph: (1 202) 712-4810; Fax: (1 202) 216-3524
http://www.info.usaid.gov
USAID addresses major micronutrient deficiencies through supplementation, food fortification, dietary modification, and intervention programmes in developing countries.

World Bank
1818 H St., NW, Washington, D.C. 20433, USA
Ph: (1 202) 458-5125; Fax: (1 202) 522-3234
E-mail: nutrition@worldbank.org
http://www.worldbank.org
The World Bank provides loans for micronutrient programmes in developing countries, with special interest in fortification programmes. The Nutrition Advisory Service provides technical services on programme design, cost effectiveness, monitoring, and evaluation of nutrition programmes.

World Health Organization (WHO)
Avenue Appia 20, CH-1211 Geneva 27, Switzerland
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ANNEX III

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ANNEX IV

Organizational Acronyms Used in the Report

AED	Academy for Educational Development
CIDA	Canadian International Development Agency
CFNI	Caribbean Food and Nutrition Institute (University of the West Indies)
ESPGAN	European Society for Paediatric Gastroenterology and Nutrition
FAO	Food and Agriculture Organization of the United Nations
GTZ	German Agency for Technical Cooperation
HKI	Helen Keller International
IOM	Institute of Medicine
INCAP	Institute of Nutrition of Central America and Panama
INTA	Institute of Nutrition and Food Technology, University of Chile
IMCI	Integrated Management of Childhood Illnesses Programme
IDRC	International Development Research Centre (Canada)
IESC	International Executive Service Corps
IFPRI	International Food Policy Research Institute
ILSI	International Life Sciences Institute
INACG	International Nutritional Anaemia Consultative Group
INF	International Nutrition Foundation
ISTI	International Science and Technology Institute
IUNS	International Union of Nutritional Sciences
IDPAS	Iron Deficiency Program Advisory Service (INF)
IWG	Iron Working Group, ACC/SCN
JHU	Johns Hopkins University
JCHP	Joint Committee on Health Policy
MI	Micronutrient Initiative
NAS	National Academy of Sciences (USA)
OMNI	Opportunities for Micronutrient Interventions
PAHO	Pan American Health Organization
PSI	Population Services International
PAMM	Program Against Micronutrient Malnutrition
PATH	Program for Appropriate Technology in Health
SCN	Subcommittee on Nutrition (UN Administrative Committee on Coordination)
SIDA	Swedish International Development Agency
ACC/SCN	United Nations Administrative Committee on Coordination, Subcommittee on Nutrition
UNDP	United Nations Development Programme
UNICEF	United Nations Children's Fund
UNU	United Nations University
USAID	United States Agency for International Development
USDA	United States Department of Agriculture
USVA	United States Veterans Administration
WB	World Bank
WFP	World Food Programme
WHO	World Health Organisation
WHO EMRO	World Health Organisation, Regional Office for the Eastern Mediterranean
WHO WPRO	World Health Organisation, Regional Office for the Western Pacific